```
? ds

Set     Items   Description
S1      32681   BISMUTH?
S2    1299336   ANTIBOD?
S3        429   S1 AND S2
S4    2153401   CANCER OR TUMOR OR MALIGNAN?
S5        147   S3 AND S4
S6         62   S5 AND PY<=1997
S7         52   RD (unique items)
S8     585995   SOLID
S9          4   S7 AND S8
S10    882783   MM??
S11         2   S7 AND S10
S12         2   RD (unique items)
? t s7/3,k,ab/1-10

 7/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09636462   98063943   PMID: 9402351
  Rapid recurrence of Helicobacter pylori infection in Peruvian patients
after successful eradication. Gastrointestinal Physiology Working Group of
the Universidad Peruana Cayetano Heredia and The Johns Hopkins University.
  Ramirez-Ramos A; Gilman RH; Leon-Barua R; Recavarren-Arce S; Watanabe J;
Salazar G; Checkley W; McDonald J; Valdez Y; Cordero L; Carrazco J
  Department of Pathology and Medicine of Universidad Peruana Cayetano
Heredia, Lima, Peru.
  Clinical infectious diseases (UNITED STATES)  Nov 1997,  25  (5)
 p1027-31,  ISSN 1058-4838  Journal Code: A4J
  Contract/Grant No.: DK 39048, DK, NIDDK
  Languages: ENGLISH
  Document type: Clinical Trial; Journal Article; Randomized Controlled
Trial
  Record type: Completed
  Helicobacter pylori is associated with gastritis, peptic ulcer disease,
and gastric cancer. Since gastric cancer is common in Peru,
eradication of H. pylori may help to reduce the occurrence of gastric
cancer . This study involved three randomized trials to determine the
efficacy of four different triple-drug therapy regimens. The most
successful regimen was furazolidone combined with bismuth
subsalicylate and amoxicillin, which eradicated infection in 82% of
patients. Patients successfully treated were followed every 2-3 months to
determine the recurrence rate of H. pylori infection. Of 105 patients with
H. pylori eradication documented by pathology and culture, 52% (55)
returned for follow-up endoscopy, and in 73% (40) of these 55 the infection
recurred during the 8-month follow-up period. Thirty-five patients from
whom H. pylori was eradicated and who were tested for antibodies to
H. pylori remained consistently seropositive. Rapid recurrence of H. pylori
infection after successful eradication suggests that measures other than
antimicrobial therapy are needed to fight H. pylori in developing
countries.

  Nov 1997,
  Helicobacter pylori is associated with gastritis, peptic ulcer disease,
and gastric cancer. Since gastric cancer is common in Peru,
eradication of H. pylori may help to reduce the occurrence of gastric
cancer . This study involved three randomized trials to determine the
efficacy of four different triple-drug therapy regimens. The most
successful regimen was furazolidone combined with bismuth
subsalicylate and amoxicillin, which eradicated infection in 82% of
patients. Patients successfully treated were followed...
... period. Thirty-five patients from whom H. pylori was eradicated and who
were tested for antibodies to H. pylori remained consistently
```

seropositive. Rapid recurrence of H. pylori infection after successful eradication...
; Adult; Aged; Amoxicillin--therapeutic use--TU; **Bismuth** --therapeutic use--TU; Drug Therapy, Combination; Follow-Up Studies; Furazolidone--therapeutic use--TU; Metronidazole--therapeutic...
Chemical Name: Anti-Infective Agents; Organometallic Compounds; Salicylates; **bismuth** subsalicylate; Tinidazole; Amoxicillin; Metronidazole; Tetracycline; Furazolidone; **Bismuth**

7/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09101426 97021921 PMID: 8868281
Evaluation of dithiol chelating agents as potential adjuvants for anti-IL-2 receptor lead or **bismuth** alpha radioimmunotherapy.
Jones SB; Tiffany LJ; Garmestani K; Gansow OA; Kozak RW
Department of Otolaryngology-Head and Neck Surgery, National Naval Medical Center, Bethesda, MD 20889, USA.
Nuclear medicine and biology (ENGLAND) Feb **1996**, 23 (2) p105-13, ISSN 0969-8051 Journal Code: BOO
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The dithiol chelating agents 2,3-dimercapto-1-propanesulfonic acid (DMPS) and meso-2,3-dimercaptosuccinic acid (DMSA) were evaluated for use as potential adjuvants to reduce or prevent radiotoxicity in anti-interleukin-2 receptor (IL-2R) Lead-212 or **Bismuth** -212 alpha-radioimmunotherapy. DMPS was less toxic than DMSA to **tumor** cell lines in culture. No adverse effects on the ability of an anti-IL-2R monoclonal **antibody** (MAb) to bind to its specific antigen were detected using DMPS or DMSA at concentrations up to 600 ug/mL in 10% or 100% mouse serum. After a 5-day oral administration of chelating agent, neither acute nor chronic toxicities on blood hematology, blood chemistry or organ weights were observed for treated mice. DMPS and DMSA were effective in accelerating whole body clearance of the gamma-emitting tracer **Bismuth** -206. Both chelates significantly reduced femur uptake of tracer when compared to nontreated control mice. However, only DMPS prevented early (2 h postinjection) renal accumulation. These studies support the use of DMPS as a potential adjuvant chelation therapy in Lead-212 or **Bismuth**-212 radioimmunotherapy protocols.

Evaluation of dithiol chelating agents as potential adjuvants for anti-IL-2 receptor lead or **bismuth** alpha radioimmunotherapy.
Feb **1996**,
... to reduce or prevent radiotoxicity in anti-interleukin-2 receptor (IL-2R) Lead-212 or **Bismuth**-212 alpha-radioimmunotherapy. DMPS was

19/3,K,AB/7 (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 1812850 IFI Acc No: 8721698
Document Type: C
MONOCLONAL **ANTIBODY** TO A HUMAN CARCINOMA **TUMOR** ASSOCIATED ANTIGEN; MURINE GENUS
Inventors: HOFHEINZ DAVID E (US); KORTRIGHT KENNETH H (US)
Assignee: COULTER CORP
Assignee Code: 11743
Publication (No,Date), Applic (No,Date):
US 4708930 **19871124** US 85702059 19850215
Publication Kind: A
Calculated Expiration: 20041124
(Cited in 025 later patents) Document Type: CERTIFICATE OF CORRECTION
Certificate of Correction Date: 19880329, 19881129
Cont.-in-part Pub(No),Applic(No,Date): ABANDONED US 84670328 19841109
Priority Applic(No,Date): US 85702059 19850215; US 84670328 19841109

Abstract: A murine monoclonal **antibody** specific for an antigenic determinant on the surface or in the cytoplasm of human carcinoma cells and tissue. A cell line is provided for producing such specific monoclonal **antibodies** for the detection, diagnosis, and therapeutic **treatment** of a plurality of human carcinomas by means of selective labelling of said monoclonal **antibodies**.

19/3,K,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06442101 88214925 PMID: 3367385
212Bismuth linked to an antipancreatic carcinoma **antibody**: model for alpha-particle-emitter radioimmunotherapy.
Kurtzman SH; Russo A; Mitchell JB; DeGraff W; Sindelar WF; Brechbiel MW; Gansow OA; Friedman AM; Hines JJ; Gamson J; et al
Surgery Branch, National Cancer Institute, Bethesda, MD 20892.
Journal of the National Cancer Institute (UNITED STATES) May 18 **1988**, 80 (6) p449-52, ISSN 0027-8874 Journal Code: J9J
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
For comparison of cytotoxicity from alpha-particle irradiation with that from conventional x-irradiation, 212Bi, an alpha-emitting radionuclide, was attached to a monoclonal **antibody** that recognizes a cell surface antigen on human pancreatic carcinoma cells. For a given level of survival, the 212Bi-**antibody** complex was found to be approximately 20 times more efficient in cell killing than x-irradiation and 5 times more cytotoxic when compared with the cytotoxicity of an antigen-negative cell line or an isotype-matched control **antibody** . High linear energy transfer radioimmunotherapy using alpha emitters linked to monoclonal **antibodies** may be useful in vivo and in vitro for selectively killing target cell populations, especially those resistant to other forms of **treatment**.

5/02

07194358 90124304 PMID: 2297751

Radioimmunotherapy of peritoneal human colon **cancer** xenografts with site-specifically modified 212Bi-labeled **antibody**.

Simonson RB; Ultee ME; Hauler JA; Alvarez VL
CYTOGEN Corporation, Princeton, New Jersey 08540.

Cancer research (UNITED STATES) Feb 1 **1990**, 50 (3 Suppl) p985s-988s, ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

212Bi is a radioisotope that emits highly cytotoxic alpha-particles. alpha-particles have a high linear energy transfer over a short path length. These properties and the 1-h half-life make this isotope suitable for radioimmunotherapy of peritoneal tumors. Therefore, we wanted to test whether monoclonal **antibodies** labeled with 212Bi would be effective in **treating** such tumors. We conjugated the **antibody** B72.3, which is reactive with many human adenocarcinomas, to the chelator linker glycyltyrosyl-lysyl-N-epsilon-diethylenetriaminepentaacetic acid, by reductive amination to the carbohydrate residues of the **antibody** (J. Rodwell, et al. Proc. Natl. Acad. Sci. USA, 83: 2632-2636, 1986). Athymic nude mice were injected i.p. with LS174T cells, a human colon **cancer** cell line. Seven to 13 days later the mice were **treated** with the 212Bi-labeled **antibody**. We **treated** the mice using single doses of 180-450 microCi or multiple doses of 80-180 microCi on consecutive days. Dissections were performed 9-16 days after the end of **treatment**. Both the single and multiple doses resulted in a decrease in **tumor** burden when compared to **tumor** from mice receiving unlabeled **antibody**. Mice in the optimum group showed **tumor** reductions of greater than 90%. **Treatment** with a 212Bi-labeled irrelevant **antibody** was significantly less effective than that with labeled B72.3 **antibody**. Survival studies showed that mice receiving the labeled **antibody** had a prolonged survival when compared to control mice.

Radioimmunotherapy of peritoneal human colon **cancer** xenografts with site-specifically modified 212Bi-labeled **antibody**.

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? ds

Set     Items   Description
S1      32681   BISMUTH?
S2    1299336   ANTIBOD?
S3        429   S1 AND S2
S4    2153401   CANCER OR TUMOR OR MALIGNAN?
S5        147   S3 AND S4
S6         62   S5 AND PY<=1997
S7         52   RD (unique items)
S8     585995   SOLID
S9          4   S7 AND S8
S10    882783   MM??
S11         2   S7 AND S10
S12         2   RD (unique items)
S13   4012047   TREAT?
S14        27   S7 AND S13
S15   4617183   LYMPHOMA OR VASCULAR OR BLOOD OR METASTA?
S16        16   S14 NOT S15
S17        16   RD (unique items)
? s helico?
     S18   76170  HELICO?
? s s17 not s18
             16  S17
          76170  S18
     S19       7  S17 NOT S18
? t s19/3,k,ab/1-7

 19/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07890184   93255137   PMID: 8488249
  A model of cell inactivation by alpha-particle internal emitters.
  Humm JL; Chin LM
  Department of Radiation Therapy, Harvard Medical School, Boston,
Massachusetts 02115.
  Radiation research (UNITED STATES)   May 1993,  134  (2)  p143-50,
ISSN 0033-7587   Journal Code: QMP
  Contract/Grant No.: 1R01-CA50886, CA, NCI
  Languages: ENGLISH
  Document type: Journal Article
  Record type: Completed
  Tumor-associated antibodies labeled with 131I and 90Y have
been used in the treatment of malignant disease with some
success. The use of alpha-particle-emitting radionuclides as radiolabels
offers potential advantages over beta-particle sources. The short range in
tissue (< 100 microns) and the high linear energy transfer associated with
alpha-particle emitters will result in a more concentrated deposition of
energy at the site of radionuclide decay. Thus, if radiolabeled
antibodies can be bound to malignant cells specifically, a high
differential cell killing can be achieved between the malignant and
the normal cells. However, the energy deposition pattern will be strongly
dependent upon the configuration of alpha-particle sources relative to the
cells, and will consequently impact upon the dose-response characteristics.
The purpose of this paper is to study distributions of energy deposition
from alpha-particle-emitting radioimmunoconjugates distributed uniformly
and nonuniformly around cells through theoretical modeling. Energy
deposition spectra for cell nuclei are calculated and used to estimate the
survival fraction by a simple biological model. We show that survival
curves resulting from nonuniform distributions of alpha-particle-emitting
radiolabeled antibodies can depart significantly from the classical
exponential survival model applied to external alpha-particle beams. The
survival curves may have initial slopes much steeper than those produced by
a uniform distribution of sources, and they may also depart from linearity.
```

Furthermore, the results of the modelling indicate how survival curves are dependent on the cell and radiolabel spacing. The results from our model compare reasonably well with published experimental data and can be used to facilitate the design and interpretation of radiobiological experiments.

May **1993**,
Tumor-associated **antibodies** labeled with 131I and 90Y have been used in the **treatment** of **malignant** disease with some success. The use of alpha-particle-emitting radionuclides as radiolabels offers potential...
... a more concentrated deposition of energy at the site of radionuclide decay. Thus, if radiolabeled **antibodies** can be bound to **malignant** cells specifically, a high differential cell killing can be achieved between the **malignant** and the normal cells. However, the energy deposition pattern will be strongly dependent upon the...

... model. We show that survival curves resulting from nonuniform distributions of alpha-particle-emitting radiolabeled **antibodies** can depart significantly from the classical exponential survival model applied to external alpha-particle beams...
; Alpha Particles; Astatine--diagnostic use--DU; Astatine--therapeutic use--TU; **Bismuth**--diagnostic use--DU; **Bismuth**--therapeutic use --TU; Computer Simulation; Dose-Response Relationship, Radiation; Models, Biological; Monte Carlo Method; Radioisotopes...
Chemical Name: Radioisotopes; Astatine; **Bismuth**

19/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07194358 90124304 PMID: 2297751
Radioimmunotherapy of peritoneal human colon **cancer** xenografts with site-specifically modified 212Bi-labeled **antibody**.
Simonson RB; Ultee ME; Hauler JA; Alvarez VL
CYTOGEN Corporation, Princeton, New Jersey 08540.
Cancer research (UNITED STATES) Feb 1 **1990**, 50 (3 Suppl) p985s-988s, ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
212Bi is a radioisotope that emits highly cytotoxic alpha-particles. alpha-p

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? s bismuth?
      S1   32681  BISMUTH?
? s antibod?
      S2 1299336  ANTIBOD?
? s s1 and s2
           32681  S1
         1299336  S2
      S3     429  S1 AND S2
? s cancer or tumor or malignan?
         1068663  CANCER
         1176691  TUMOR
          455166  MALIGNAN?
      S4 2153401  CANCER OR TUMOR OR MALIGNAN?
? s s3 and s4
             429  S3
         2153401  S4
      S5     147  S3 AND S4
? s s5 and py<=1997
Processing
Processing
             147  S5
        31406065  PY<=1997
      S6      62  S5 AND PY<=1997
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...examined 50 records  (50)
...completed examining records
      S7      52  RD (unique items)
? s solid
      S8  585995  SOLID
? s s7 and s8
             52  S7
         585995  S8
      S9       4  S7 AND S8
? t s9/3,k,ab/1-4

 9/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08797787   95405762   PMID: 7675360
  Cytotoxicity of 213Bi- and 225Ac-immunoconjugates.
  Kaspersen  FM; Bos E; Doornmalen AV; Geerlings MW; Apostolidis C; Molinet
R
  NV Organon, Oss.
  Nuclear  medicine  communications (ENGLAND)  Jun  1995,  16  (6)
 p468-76,  ISSN 0143-3636  Journal Code: OB8
  Languages: ENGLISH
  Document type: Journal Article
  Record type: Completed
  This  paper  describes  in vitro cytotoxicity experiments with 213Bi- and
225Ac-immunoconjugates  on the human epidermoid tumour cell line A431 using
a  blood  group A-reactive murine IgG (2D11) as the specific antibody
 and  MOPC  21  as  the  control  antibody . With both radionuclides,
specific  cell-killing  was  achieved.  The  observed cytotoxicity of 213Bi
(T1/2  -  47  min) indicates that this radionuclide is a useful alternative
for  the  alpha-emitter  212Bi  in  the  treatment  of  blood-borne
malignancies .  225Ac-immunoconjugates (T1/2 of 225Ac is 10 days) may
be  applicable for the treatment of solid tumours, since the daughter
radionuclides  of  225Ac  contribute  to  the cytotoxic efficacy by a field
effect  (i.e.  toxicity  in  an area distal from the antibody-binding
site). The lack of an adequate chelator for 225Ac is a major drawback.
```

Jun **1995**,

...cell line A431 using a blood group A-reactive murine IgG (2D11) as the specific **antibody** and MOPC 21 as the control **antibody**. With both radionuclides, specific cell-killing was achieved. The observed cytotoxicity of 213Bi (T1/2...

... is a u

```
? ds

Set     Items   Description
S1      32681   BISMUTH?
S2    1299336   ANTIBOD?
S3        429   S1 AND S2
S4    2153401   CANCER OR TUMOR OR MALIGNAN?
S5        147   S3 AND S4
S6         62   S5 AND PY<=1997
S7         52   RD (unique items)
S8     585995   SOLID
S9          4   S7 AND S8
? s mm??
     S10  882783  MM??
? s s7 and s10
               52  S7
           882783  S10
     S11       2  S7 AND S10
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S12       2  RD (unique items)
? t s12/3,k,ab/1-2

 12/3,K,AB/1     (Item 1 from file: 34)
DIALOG(R)File  34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

06361294   Genuine Article#: YM158   Number of References: 15
Title: A gamma detector probe with ex vivo detection of carcinoi
```

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? s bismuth(w)213 or bi(w)213
          31926  BISMUTH
          14767  213
            100  BISMUTH(W)213
         563581  BI
          14767  213
            122  BI(W)213
      S1    202  BISMUTH(W)213 OR BI(W)213
? s tumor? or cancer? or malignan? or carcinoma??
Processing
        1434379  TUMOR?
        1107543  CANCER?
         453939  MALIGNAN?
         725946  CARCINOMA??
      S2 2579937  TUMOR? OR CANCER? OR MALIGNAN? OR CARCINOMA??
? s bismuth213
      S3       0  BISMUTH213
? s s1 and s2
             202  S1
         2579937  S2
      S4     121  S1 AND S2
? s antibod?
      S5 1296548  ANTIBOD?
? s s4 and s5
             121  S4
         1296548  S5
      S6      90  S4 AND S5
? s s6 and py<=1997
Processing
Processing
              90  S6
        31405898  PY<=1997
      S7       8  S6 AND PY<=1997
? t s7/3,k,ab/1-8

 7/3,K,AB/1     (Item 1 from file: 55)
DIALOG(R)File  55:Biosis Previews(R)
(c) 2002 BIOSIS. All rts. reserv.

11105521   BIOSIS NO.: 199799726666
Antibody targeted high energy alpha particle therapy: Development and
  use of a bismuth-213-humanized anti-CD33 agent.
AUTHOR: Scheinberg David A; Jurcic Joseph G; McDevitt Michael; Finn Ronald;
  Larson Steven M; Gerrlings Mauritz Jr; Curcio Michael; Sgouros George(a);
  Gansow Otto; Breitbeil Martin; Geerlings Mauritz Sr; Apostolidis Christos
AUTHOR ADDRESS: (a)Memorial Sloan-Kettering Cancer Center, 1275 York Ave.,
  New York, NY 10021**USA
JOURNAL: AAAS Annual Meeting and Science Innovation Exposition  163 (0):p
A50 1997
CONFERENCE/MEETING: 163rd National Meeting of the American Association for
the Advancement of Science: Engaging Science, Sustaining Society  Seattle,
Washington, USA  February 13-18, 1997
RECORD TYPE: Citation
LANGUAGE: English
1997

Antibody targeted high energy alpha particle therapy: Development and
  use of a bismuth-213-humanized anti-CD33 agent.
1997
  MISCELLANEOUS TERMS:    ...ANTIBODY TARGETED HIGH ENERGY ALPHA
    PARTICLE THERAPY...

...BISMUTH-213-HUMANIZED ANTI-CD33 AGENT...
```

...**CANCER**; ...

...**TUMOR** BIOLOGY

7/3,K,AB/2 (Item 2 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)

4/23

09912486 BIOSIS NO.: 199598367404
Cytotoxicity of 213Bi- and 225Ac-immunoconjugates.
AUTHOR: Kaspersen F M; Bos E(a); Doornmalen A V; Geerlings M W; Apostolidis C; Molinet R
AUTHOR ADDRESS: (a)NV Organon, P.O. Box 20, 5340 BH Oss**Germany
JOURNAL: Nuclear Medicine Communications 16 (6):p468-476 **1995**
ISSN: 0143-3636
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: This paper describes in vitro cytotoxicity experiments with 213Bi- and 225Ac-immunoconjugates on the human epidermoid tumour cell line A431 using a blood group A-reactive murine IgG (2D11) as the specific **antibody** and MOPC 21 as the control **antibody**. With both radionuclides, specific cell-killing was achieved. The observed cytotoxicity of 213Bi (T-1/2 = 47 min) indicates that this radionuclide is a useful alternative for the alpha-emitter 212Bi in the treatment of blood-borne **malignancies**. 225Ac-immunoconjugates (T-1/2 of 225Ac is 10 days) may be applicable for the treatment of solid tumours, since the daughter radionuclides of 225Ac contribute to the cytotoxic efficacy by a field effect (i.e. toxicity in an area distal from the **antibody** -binding site). The lack of an adequate chelator for 225Ac is a major drawback.

1995

1995

...ABSTRACT: cell line A431 using a blood group A-reactive murine IgG (2D11) as the specific **antibody** and MOPC 21 as the control **antibody**. With both radionuclides, specific cell-killing was achieved. The observed cytotoxicity of 213Bi (T-1...

...is a useful alternative for the alpha-emitter 212Bi in the treatment of blood-borne **malignancies**. 225Ac-immunoconjugates (T-1/2 of 225Ac is 10 days) may be applicable for the...

...cytotoxic efficacy by a field effect (i.e. toxicity in an area distal from the **antibody**-binding site). The lack of an adequate chelator for 225Ac is a major drawback.
...REGISTRY NUMBERS: **BISMUTH-213**;
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: **BISMUTH-213**;
MISCELLANEOUS TERMS: ...**ANTIBODY**; ...

...**BISMUTH-213**;

7/3,K,AB/3 (Item 3 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)

08999430 BIOSIS NO.: 199497007800

decreased to 60% at an average of 3.5 chelators per molecule, the 60% level was obtained at an average of 6.5 chelators per streptavidin molecule. Streptavidin may therefore possibly be used to obtain Bi-212, **Bi-213**-labelled compounds for alpha-particle radiotherapy with higher specific activity.

Title: Bi-labelled **antibody** and bi-labelled streptavidin. Comparison of targeting efficacy of a lymphoma cell line in vitro
, **1997**
Abstract: An anti-lymphoma **antibody** (HH-1) and streptavidin were conjugated with the chelator CHX-A DTPA add subsequently labelled with Bi-205,Bi-206. The immunoreactivity of the **antibody** to the target antigen and the binding ability of streptavidin to antigen-bound biotinylaled HH...

...5 chelators per streptavidin molecule. Streptavidin may therefore possibly be used to obtain Bi-212,**Bi-213**-labelled compounds for alpha-particle radiotherapy with higher specific activity.
...Identifiers--BIOTINYLATED MONOCLONAL-**ANTIBODIES**; RADIOLABELED STREPTAVIDIN; RADIOIMMUNOTHERAPY; ASTATINE-211; BINDING; AVIDIN; **TUMOR**; TAC

7/3,K,AB/6 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04079741 Genuine Article#: RC713 Number of References: 0
(NO REFS KEYED)
Title: CYTOTOXICITY OF **BI-213**-IMMUNOCONJUGATES AND AC-225-IMMUNOCONJUGATES (Abstract Available)
Author(s): KASPERSEN FM; BOS E; DOORNMALEN AV; GEERLINGS MW; APOSTOLIDIS C; MOLINET R
Corporate Source: NV ORGANON,POB 20/5340 BH OSS//NETHERLANDS/; NV ORGANON/5340 BH OSS//NETHERLANDS/
Journal: NUCLEAR MEDICINE COMMUNICATIONS, **1995**, V16, N6 (JUN), P 468-476
ISSN: 0143-3636
Language: ENGLISH Document Type: ARTICLE
Abstract: This paper describes in vitro cytotoxicity experiments with **Bi-213**- and Ac-225-immunoconjugates on the human epidermoid tumour cell line A431 using a blood group A-reactive murine IgG (2D11) as the specific **antibody** and MOPC 21 as the control **antibody**. With both radionuclides, specific cell-killing was achieved. The observed cytotoxicity of **Bi-213** (T-1/2 = 47 min) indicates that this radionuclide is a useful alternative for the alpha-emitter Bi-212 in the treatment of blood-borne **malignancies** . Ac-225-immunoconjugates (T-1/2 of (225)AC is 10 days) may be applicable for the treatment of solid rumours, since the daughter radionuclides of (225)AC contribute to the cytotoxic efficacy by a field effect (i.e. toxicity in an area distal from the **antibody** -binding site). The lack of an adequate chelator for (225)AC is a major drawback.

Title: CYTOTOXICITY OF **BI-213**-IMMUNOCONJUGATES AND AC-225-IMMUNOCONJUGATES
, **1995**
Abstract: This paper describes in vitro cytotoxicity experiments with **Bi-213**- and Ac-225-immunoconjugates on the human epidermoid tumour cell line A431 using a blood group A-reactive murine IgG (2D11) as the specific **antibody** and MOPC 21 as the control **antibody**. With both radionuclides, specific cell-killing was achieved. The observed cytotoxicity of **Bi-213** (T-1/2 = 47 min) indicates that this radionuclide is a useful alternative for the

alpha-emitter Bi-212 in the treatment of blood-borne **malignancies** . Ac-225-immunoconjugates (T-1/2 of (225)AC is 10 days) may be applicable...

...cytotoxic efficacy by a field effect (i.e. toxicity in an area distal from the **antibody**-binding site). The lack of an adequate chelator for (225)AC is a major drawback.

7/3,K,AB/7 (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 2680208 IFI Acc No: 9600860
Document Type: C
DETECTION AND THERAPY OF LESIONS WITH BIOTIN/AVIDIN POLYMER CONJUGATES
Inventors: Griffiths Gary L (US)
Assignee: Immunomedics Inc
Assignee Code: 14427
Publication (No,Date), Applic (No,Date):
US 5482698 **19960109** US 9351144 19930422
Publication Kind: A
Calculated Expiration: 20130422
(Cited in 010 later patents)
Priority Applic(No,Date): US 9351144 19930422

Abstract: Methods of detecting and/or treating lesions in a patient are provided. The methods are an improvement over known methods comprising the steps of (a) parenterally injecting a subject with a targeting composition comprised of a biotin-protein conjugate or an avidin-protein conjugate, wherein the protein preferentially binds to a marker substance produced or associated with the targeted lesion, and allowing the protein conjugate to preferentially accrete at the targeted lesion; (b) then parenterally injecting a clearing composition comprised of (i) avidin, when the targeting composition is a biotin-protein conjugate, or (ii) biotin, when the targeting composition is a avidin-protein conjugate, and allowing the clearing composition to substantially clear the targeting composition from nontargeted sites and to bind to the targeting composition accreted at the targeted lesion; and (c) parenterally injecting a detection or therapeutic composition comprised of a conjugate of (i) avidin and detection or therapeutic agent when the clearing composition is biotin, or (ii) biotin and detection or therapeutic agent when the clearing agent is avidin, and allowing the composition to accrete at the targeted lesion. The improvement is having at least one of the compositions of step (a) or (b) further comprise a polymer to which multiple moieties of avidin or biotin can conjugate, thereby providing an increased number of binding sites to which a subsequently administrated composition can bind thereby amplifying the amount of detection or therapeutic agent at the targeted site.

Publication (No,Date), Applic (No,Date):
...**19960109**
Non-exemplary Claims: ...14. The method of claim 1, wherein the lesion is **cancerous**, cardiovascular, infectious or inflammatory...

...16. The method of claim 14, wherein the **cancerous** lesion is a **carcinoma**, melanoma, sarcoma, neuroblastoma, leukemia, lymphoma, glioma or myeloma...

...of a peptide, polypeptide, hormone, lymphokine, growth factor, albumin, cytokine, enzyme, immune modulator, receptor protein, **antibody** and **antibody** fragment...

...19. The method of claim 18, wherein the protein is one of monoclonal

antibody, or a specific binding fragment thereof...

...The method of claim 19, wherein the fragment is one of a Fv, single chain **antibody**, Fab, Fab', F(ab)2 or F(ab')2...

...22. The method of claim 19, wherein the **antibody** is multispecific ...

...23. The method of claim 22, wherein the **antibody** is multispecific to differing epitopes or molecules of a marker substance...is an isotope which is one of Iodine-125, Iodine-131, Actinium-225, Bismuth-212, **Bismuth-213**, Lead-212, Rhenium-186, Rhenium-188, Silver-111, Platinum-197, Palladium-109, Copper-67, Phosphorus...

7/3,K,AB/8 (Item 2 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 1528011 IFI Acc No: 8410307
Document Type: C
USE OF METAL CHELATE CONJUGATED MONOCLONAL **ANTIBODIES**; DIAGNOSIS, TREATMENT OF **CANCER**
Inventors: GANSOW OTTO A (US); STRAND METTE (US)
Assignee: UNASSIGNED OR ASSIGNED TO INDIVIDUAL
Assignee Code: 68000 Document Type: REASSIGNED
Publication (No,Date), Applic (No,Date):
US 4454106 **19840612** US 82386109 19820607
Publication Kind: A
Calculated Expiration: 20020607
(Cited in 071 later patents) Document Type: CERTIFICATE OF CORRECTION
Certificate of Correction Date: 19841120
Priority Applic(No,Date): US 82386109 19820607

Abstract: Therapeutic and diagnostic methods employing metal chelate conjugated monoclonal **antibodies** are described. Metals employed in therapeutic conjugated **antibodies** include alpha particle, beta particle or Auger electron emitting isotopes. Diagnostic methods may be either in vivo or in vitro. Chelated metals employed in diagnostic techniques may include, inter alia, gamma or positron emitting metals as well as fluorogenic or paramagnetic metals.

USE OF METAL CHELATE CONJUGATED MONOCLONAL **ANTIBODIES**; ...

...DIAGNOSIS, TREATMENT OF **CANCER**
Publication (No,Date), Applic (No,Date):
...**19840612**

Abstract: Therapeutic and diagnostic methods employing metal chelate conjugated monoclonal **antibodies** are described. Metals employed in therapeutic conjugated **antibodies** include alpha particle, beta particle or Auger electron emitting isotopes. Diagnostic methods may be either...

Exemplary Claim: ...METHOD COMPRISING INTRODUCING INTO BODY FLUID A SOLUTION OF METAL DIETHYLENETRIAMINEPENTAACETIC ACID CHELATE CONJUGATED MONOCLONAL **ANTIBODIES** WHEREIN SAID METAL IS SELECTED FROM THE GROUP CONSISTING OF PARAMAGNETIC METALS, GAMMA EMITTING METALS...

...SAID CONJUGATE HAS AT LEAST ABOUT 80% OF THE BIOLOGICAL ACTIVITY AND SELECTIVITY OF THE **ANTIBODY**.
18. AN IN VITRO DIAGNOSTIC METHOD COMPRISING INTRODUCING INTO A TEST MEDIUM A SOLUTION OF METAL DIETHYLENETRIAMINEPENTAACETIC ACID CHELATE

CONJUGATED MONOCLONAL **ANTIBODIES** AND QUANTIFYING THE SPECIFICALLY BOUND PORTION OF SAID CONJUGATE, SAID METAL BEING SELECTED FROM THE...

...SAID CONJUGATE HAVING AT LEAST ABOUT 80% OF THE BIOLOGICAL ACTIVITY AND SPECIFICITY OF THE **ANTIBODY**.

Non-exemplary Claims: ...treating cellular disorders comprising introducing into body fluid a solution of radiometal chelate conjugated monoclonal **antibodies** specific for a target cell, said radiometal being an alpha, beta or Auger electron emitter...

...substantially all of said radiometal in said solution being chelated by said chelate conjugated monoclonal **antibodies**.

...

...wherein said radiometal is selected from the group consisting of Bi-211, Bi-212 and **Bi-213**.

...

...6. The method of claim 2 wherein said chelate conjugated monoclonal **antibodies** are produced from a carboxycarbonic anhydride of diethylenetriaminepentaacetic acid and a monoclonal **antibody**.

...

...8. The method of claim 5 wherein said radiometal chelate conjugated monoclonal **antibody** solution has at least about 94% of the radiometal bound by the chelate and said conjugate retains at least about 80% of the biological activity and specificity of the **antibody**.

...

...of claim 6 wherein said radiometal is Bi-212 and the metal chelate conjugated monoclonal **antibody** solution has at least about 98% of the radiometal bound by the chelate and said conjugate retains at least about 95% of the biological activity and specificity of the **antibody**.

...

...disorders comprising introducing into body fluid a solution of radiometal diethylenetriaminepentaacetic acid chelate conjugated monoclonal **antibodies** wherein said radiometal is selected from the group consisting of beta emitting radiometals and Auger...

...said conjugate having at least about 80% of the biological activity and specificity of the **antibody**.

...

...12. The method of claim 10 wherein said conjugated **antibody** is produced from a carboxycarbonic anhydride of diethylenetriaminepentaacetic acid and a monoclonal **antibody**.

...

...said conjugate retains at least about 95% of the biological activity and specificity of the **antibody**.

...

...said conjugate retains at least about 95% of the biological activity and specificity of the **antibody**.

...

...said conjugate retains at least about 95% of the biological activity and specificity of the **antibody**.

?

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? s (solid or bulky) (5n) (tumor or cancer or malignan? or carcinoma??)
          584255  SOLID
           16610  BULKY
         1172640  TUMOR
         1064779  CANCER
          453939  MALIGNAN?
          725946  CARCINOMA??
      S1   20601  (SOLID OR BULKY) (5N) (TUMOR OR CANCER OR MALIGNAN? OR
                  CARCINOMA??)
? s alpha (5n) (particle?? or isotope or radio?)
>>>File 155 processing for RADIO? stopped at RADIOIMMUNOABSORBENT
>>>File 55 processing for RADIO? stopped at RADIOVISIOGRAPH
>>>File 34 processing for RADIO? stopped at RADIOPHYSICISTS
         1425951  ALPHA
          639359  PARTICLE??
           98883  ISOTOPE
         1218936  RADIO?
      S2   19121  ALPHA (5N) (PARTICLE?? OR ISOTOPE OR RADIO?)
? s s1 and s2
           20601  S1
           19121  S2
      S3      28  S1 AND S2
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
      S4      19  RD (unique items)
? s s4 and py<=1998
Processing
Processing
              19  S4
        33496514  PY<=1998
      S5      11  S4 AND PY<=1998
? t s5/3,k,ab/1-11

 5/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
```

9/23

10296146 98090340 PMID: 9430475

Radioimmunotherapy targeting of HER2/neu oncoprotein on ovarian tumor using lead-212-DOTA-AE1.

Horak E; Hartmann F; Garmestani K; Wu C; Brechbiel M; Gansow OA; Landolfi NF; Waldmann TA

Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.

Journal of nuclear medicine (UNITED STATES) Dec **1997**, 38 (12) p1944-50, ISSN 0161-5505 Journal Code: JEC

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

The specificity, toxicity and efficacy of lead (212Pb) radioimmunotherapy were evaluated in nude mice bearing the SK-OV-3 human ovarian tumor cell line expressing the HER2/neu proto-oncogene. METHODS: The therapeutic agent used was the tumor-specific anti-HER2/neu monoclonal antibody AE1 conjugated to 212Pb, 212Bi being the daughter and thus the source of the **alpha-particle** and beta emissions. A bifunctional derivative of tetraazacyclododecanetetraacetic acid (p-SCN-Bz-DOTA) was used to couple 212Pb to the anti-HER2/neu monoclonal antibody AE1. The chelating agent did not alter the binding affinity to its antigenic target or the pharmacokinetics and tissue distribution of the AE1 antibody. Toxicity and therapeutic efficacy of 212Pb-AE1 were evaluated in nude mouse ascites or **solid tumor** models, wherein SK-OV-3 cells were administered

i.p. or s.c., respectively. RESULTS: The dose-limiting acute toxicity after i.v. administration of 212Pb-AE1 was bone marrow suppression, which was observed at doses above 25 microCi. Therefore, doses of 10 and 20 microCi were used in efficacy trials. The i.p. administration of 212Pb-AE1 3 days after i.p. tumor inoculation led to a significant (P2 = 0.015) prolongation of tumor-free survival. In a second model, i.v. treatment with 212Pb-AE1 3 days after s.c. tumor inoculation prevented subsequent tumor development in all animals treated with 10 or 20 microCi of 212Pb-AE1 (P2 = 0.002 compared to control groups). This efficacy in the adjuvant setting was antibody specific because treatments with equivalently labeled control antibody or unlabeled AE1 antibody or no treatment were less effective. The rate of growth of small (mean tumor volume, 15 mm3) SK-OV-3 tumors was modestly inhibited. However, tumor growth was not inhibited in mice bearing larger (mean tumor volume, 146 mm3) SK-OV-3 tumors by the administration of a single dose of 10 or 20 microCi of 212Pb-AE1. CONCLUSION: Lead-212-AE1 as an intact radiolabeled monoclonal antibody may be of only modest value in the therapy of bulky solid tumors due to the short physical half-life of 212Pb and time required to achieve a useful tumor-to-normal tissue ratio of radionuclide after administration. However, the radiolabeled monoclonal antibody may be useful in therapy of tumors in the adjuvant setting. Furthermore, 212Pb may be of value in select situations, including treatment of leukemia, intercavitary therapy or strategies that target vascular endothelial cells of tumors.

Dec **1997**,
... antibody AE1 conjugated to 212Pb, 212Bi being the daughter and thus the source of the **alpha-particle** and beta emissions. A bifunctional derivative of tetraazacyclododecanetetraacetic acid (p-SCN-Bz-DOTA) was used...

... antibody. Toxicity and therapeutic efficacy of 212Pb-AE1 were evaluated in nude mouse ascites or **solid tumor** models, wherein SK-OV-3 cells were administered i.p. or s.c., respectively. RESULTS...

5/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

4/23

08203736 94320068 PMID: 8044783
Radioimmunotherapy of nude mice bearing a human interleukin 2 receptor alpha-expressing lymphoma utilizing the alpha-emitting radionuclide-conjugated monoclonal antibody 212Bi-anti-Tac.
Hartmann F; Horak EM; Garmestani K; Wu C; Brechbiel MW; Kozak RW; Tso J; Kosteiny SA; Gansow OA; Nelson DL; et al
Metabolism Branch, National Cancer Institute, NIH, Bethesda, Maryland 20892.
Cancer research (UNITED STATES) Aug 15 **1994**, 54 (16) p4362-70, ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The efficacy, specificity, and toxicity of bismuth (212Bi) **alpha particle** -mediated radioimmunotherapy was evaluated in nude mice bearing a murine lymphoma transfected with the human CD25 [human Tac; interleukin 2 receptor alpha (IL-2R alpha)] gene. The therapeutic agent used was the tumor-specific humanized monoclonal antibody anti-Tac conjugated to 212Bi. The human IL-2R alpha-expressing cell line was produced by transfecting the gene encoding human Tac into the murine plasmacytoma cell line SP2/0. The resulting cell line, SP2/Tac, expressed approximately 18,000 human IL-2R alpha molecules/cell. Following s.c. or i.p. injection of 2 x 10(6) SP2/Tac cells into nude mice, rapidly growing tumors developed in all animals after a mean of 10 and 13 days, respectively. The bifunctional chelate cyclohexyldiethylenetriaminepentaacetic acid was used to couple 212Bi to the humanized anti-Tac monoclonal

antibody. This immunoconjugate was shown to be stable in vivo. Specifically, in pharmacokinetic studies in nude mice, the blood clearance patterns of i.v. administered 205/206Bi-anti-Tac and coinjected 125I-anti-Tac were comparable. The toxicity and therapeutic efficacy of 212Bi-anti-Tac were evaluated in nude mouse ascites or **solid tumor** models wherein SP2/Tac cells were administered either i.p. or s.c., respectively. The i.p. administration of 212Bi-anti-Tac, 3 days following i.p. tumor inoculation, led to a dose-dependent, significant prolongation of tumor-free survival. Doses of 150 or 200 microCi prevented tumor occurrence in 75% (95% confidence interval, 41-93%) of the animals. In the second model, i.v. treatment with 212Bi-anti-Tac 3 days following s.c. tumor inoculation also resulted in a prolongation of the period before tumor development. However, prevention of tumor occurrence decreased to 30% (95% confidence interval, 11-60%). In both the i.p. and s.c. tumor trials, 212Bi-anti-Tac was significantly more effective for i.p. (P2 = 0.0128 50/100 microCi 212Bi-anti-Tac versus 50/100 microCi Mik beta; P2 = 0.0142 150/200 microCi anti-Tac versus 150/200 microCi Mik beta) and for s.c. tumors (P2 = 0.0018 100 microCi anti-Tac versus 100 microCi Mik beta; P2 = 0.0042 200 microCi anti-Tac versus 200 microCi Mik beta 1) than the control antibody Mik beta 1 coupled to 212Bi at comparable dose levels. In contrast to the efficacy observed in the adjuvant setting, therapy of large, established s.c. SP-2/Tac-expressing tumors with i.v. administered 212Bi-anti-Tac (at doses up to 200 microCi/animal) failed to induce tumor regression.(ABSTRACT TRUNCATED AT 400 WORDS)

Aug 15 **1994**,

The efficacy, specificity, and toxicity of bismuth (212Bi) **alpha particle** -mediated radioimmunotherapy was evaluated in nude mice bearing a murine lymphoma transfected with the human...

... toxicity and therapeutic efficacy of 212Bi-anti-Tac were evaluated in nude mouse ascites or **solid tumor** models wherein SP2/Tac cells were administered either i.p. or s.c., respectively. The...

5/3,K,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

4/23

06553268 89092141 PMID: 2910786

The effect of the alpha-emitting radionuclide lead-212 on human ovarian carcinoma: a potential new form of therapy.

Rotmensch J; Atcher RW; Schlenker R; Hines J; Grdina D; Block BS; Press MF; Herbst AL; Weichselbaum RR

Department of Obstetrics and Gynecology, University of Chicago, Pritzker School of Medicine, Illinois 60637.

Gynecologic oncology (UNITED STATES) Feb **1989**, 32 (2) p236-9, ISSN 0090-8258 Journal Code: FXC

Contract/Grant No.: 5 RO1 CA-37436, CA, NCI; CA-27476, CA, NCI

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

To improve response and survival of patients with ovarian carcinoma noncross-resistant forms of therapy must be developed. alpha-emitting radionuclides may be therapeutically useful since they can directly ionize with energies of 5 to 9 MeV, penetrate only a few cell diameters, and transfer a high amount of energy. The purpose of this study was to determine the effect of the alpha-emitter, lead-212 (212Pb), complexed to sulfur in a nude athymic mouse model (NIH:OVCAR-3) containing human ascites and **solid** epithelial ovarian **carcinoma**. Thirty-six nude mice 28 to 32 days old were injected with 10(7) to 10(8) carcinoma cells from donor mice. After 4 weeks, six groups of six nu/nu athymic BALB-C mice were intraperitoneally injected with 70, 50, 20, 5 microCi of 212Pb sulfur colloid, sulfur colloid, or saline. Tumor necrosis with a decrease in ascites and a dose-related survival were noted with doses of 50, 20, and 5

microCi. With 70 microCi acute gastrointestinal toxicity developed. These experiments form the basis for further investigations and the development of **alpha**-emitting **radiocolloids** which may be of therapeutic efficacy in the treatment of intraperitoneal ovarian carcinoma.

Feb **1989**,
...to sulfur in a nude athymic mouse model (NIH:OVCAR-3) containing human ascites and **solid** epithelial ovarian **carcinoma**. Thirty-six nude mice 28 to 32 days old were injected with 10(7) to...

... gastrointestinal toxicity developed. These experiments form the basis for further investigations and the development of **alpha**-emitting **radiocolloids** which may be of therapeutic efficacy in the treatment of intraperitoneal ovarian carcinoma.

5/3,K,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06326557 88016864 PMID: 3659271
Analytical techniques for boron and boron 10 analysis in a **solid** experimental **tumor** EO. 771.
Porschen W; Marx J; Dallacker F; Muckter H; Bohmel T; Fairchild R; Feinendegen LE
Institut fur Medizin, Kernforschungsanlage GmbH, Julich, Federal Republic of Germany.
Radiation and environmental biophysics (GERMANY, WEST) **1987**, 26 (3) p209-18, ISSN 0301-634X Journal Code: QML
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
If a tumor can be preferentially loaded with a suitable boron-10 compound and irradiated with thermal neutrons, malignant cells can be selectively destroyed via the **alpha-particle** + Li 7-nucleus from the reaction 10B(n, alpha)7Li. Neutron capture therapy with two boron-10 amino acid analogs of low toxicity has been tested in recent years: (a) trimethylamine-carboxyborane, (A3) and (b) amine-carboxyborane, (A7). Now the boron-10 glycineamide analog (A8), amineboryl-carboxamide has been synthesized; it contains 13.81% boron (90% Boron 10 + 10% Boron 11) and shows a very low toxicity in mice. The effects of this compound were tested on the syngeneic solid adenocarcinoma EO 771 on the right hind leg of male C57 BL/6J mice under standard conditions, by measuring tumor volume growth delay and cell cycle changes using flow cytometry. Boron distribution between tumor and muscle was analyzed by emission spectroscopy with inductively coupled plasma (ICP) following injection of a suspension of peanut oil emulsion. In addition, boron-10 concentration in the tumor were analyzed with prompt gamma-activation analysis and neutron capture radiography (Kodak-Pathe LR 115) at the MRR reactor in Brookhaven after i.p. injection of 0.4 mg/g A8. Application of A8 alone (0.4 mg/g i.p.) or thermal neutron irradiation of the tumor EO. 771 produced a tumor growth delay of 1-2 days for tumor volume doubling. Application of the boron 10 glycine-amide analog A8 i.p. plus 5 X 10(12)n/cm2 resulted in a growth delay of 3-6 days. In contrast intratumoral application of A8 plus 4 X 10(12)n/cm2 neutrons gave a growth delay of 7-14 days; the fraction of (G2 + M) cells rose from 35% (neutrons alone) to 52%, as evaluated from flow cytometry.

Analytical techniques for boron and boron 10 analysis in a **solid** experimental **tumor** EO. 771.
1987,
... 10 compound and irradiated with thermal neutrons, malignant cells can be selectively destroyed via the **alpha-particle** + Li 7-nucleus from the reaction 10B(n, alpha)7Li. Neutron capture therapy with two...

5/3,K,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02435529 77128754 PMID: 841610
[In-vivo-examinations of the relative radiosensitivity of hypoxic tumor cells (author's transl)]
In-vivo-Untersuchungen uber die relative Strahlenempfindlichkeit hypoxischer Tumorzellen
Bosiljanoff P; Porschen W; Piepenbring W; Muhlensiepen H; Feinendegen LE
Strahlentherapie (GERMANY, WEST) Mar **1977**, 153 (3) p178-89,
ISSN 0039-2073 Journal Code: V1Z
Languages: GERMAN
Document type: Journal Article
Record type: Completed
The rate of cellular losses of hypoxic respectively euoxic cells of the **solid** experimental **tumor** "sarcoma 180" was examined in vivo after irradiations with gamma rays, 15 MeV neutrons, and **alpha particles** . The tumor cells were labeled in vivo, at first with 125I-UdR and after 50 hours with 131I-UdR. After a further interval of about 20 hours the tumor was irradiated. This method of double labeling makes it possible to determine externally the rates of cellular losses in the labeled zones of tumor cells presenting different partial oxygen pressures. The increase of the rates of cellular losses among the euoxic and hypoxic tumor cells induced by the gamma radiation differs by 2.6; it decreases, however, to 1.5 after injection of nitrofurazone prior to the irradiation. After irradiation with 15 MeV neutrons, a difference of only 1.4 was observed. If the tumors were irradiated internally with **alpha particles** from the reaction 10B(n,**alpha**) 7Li, there was no difference between the two rates of cellular losses. As far as the above mentioned kinds of radiation are concerned, the ratios from the increase of the rates of cellular losses induced by radiation are well corresponding to the oxygen enhancement found by other authors during their examinations in vitro.

Mar **1977**,
The rate of cellular losses of hypoxic respectively euoxic cells of the **solid** experimental **tumor** "sarcoma 180" was examined in vivo after irradiations with gamma rays, 15 MeV neutrons, and **alpha particles** . The tumor cells were labeled in vivo, at first with 125I-UdR and after 50...

... a difference of only 1.4 was observed. If the tumors were irradiated internally with **alpha particles** from the reaction 10B(n, **alpha**) 7Li, there was no difference between the two rates of cellular losses. As far as...
; **Alpha Particles**; Cell Count; Deoxyuridine; Gamma Rays; Iodine Radioisotopes; Mice; Neutrons; Oxygen; Oxygen Consumption--radiation effects--RE...

5/3,K,AB/6 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06616100 Genuine Article#: ZE898 Number of References: 29
Title: Vascular targeted **radioimmunotherapy** with Bi-213 - An **alpha-particle** emitter (ABSTRACT AVAILABLE)
Author(s): Kennel SJ (REPRINT) ; Mirzadeh S
Corporate Source: OAK RIDGE NATL LAB,DIV LIFE SCI, POB 2009/OAK RIDGE//TN/37831 (REPRINT)
Journal: NUCLEAR MEDICINE AND BIOLOGY, **1998**, V25, N3 (APR), P241-246
ISSN: 0969-8051 Publication date: 19980400
Publisher: ELSEVIER SCIENCE INC, 655 AVENUE OF THE AMERICAS, NEW YORK, NY

10010
Language: English Document Type: ARTICLE
Abstract: To destroy both tumor blood vessels and adjacent tumor cells, an cu particle emitter, Bi-213, has been targeted with a monoclonal antibody (MAb) to vessels that feed lung tumors in mice. Animals, bearing approximately 100 EMT-6 carcinomas each of 50-400 cells in size in the lung, that were treated with 120 mu Ci of Bi-213-MAb 201B were all cured of their disease, Animals treated when tumors were larger (10(3)-10(4) cells) had extended life spans, but a small number of residual tumors eventually killed the animals. Significant extension of life span was also induced with another tumor model - rat tracheal carcinoma growing in the lungs of SCID mice that were then treated with 136 mu Ci Bi-213-MAb B-201. These studies indicate that attack of both blood vessels and tumor cells simultaneously is an effective mode of cancer treatment. (C) 1998 Elsevier Science Inc.

Title: Vascular targeted **radioimmunotherapy** with Bi-213 - An **alpha-particle** emitter
, **1998**
...Identifiers--MONOCLONAL-ANTIBODIES; **TUMOR**-GROWTH; ENDOTHELIAL-CELLS; EPITHELIAL-CELLS; **SOLID** TUMORS; INHIBITION; ANGIOGENESIS; THERAPY; METASTASIS; INVIVO

5/3,K,AB/7 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06492753 Genuine Article#: YW901 Number of References: 30
Title: Vascular targeting for radioimmunotherapy with Bi-213 (ABSTRACT AVAILABLE)
Author(s): Kennel SJ (REPRINT) ; Mirzadeh S
Corporate Source: OAK RIDGE NATL LAB,DIV LIFE SCI/OAK RIDGE//TN/37831 (REPRINT)
Journal: RADIOCHIMICA ACTA, **1997**, V79, N2, P87-91
ISSN: 0033-8230 Publication date: 19970000
Publisher: R OLDENBOURG VERLAG, LEKTORAT M/N, K BERBER-NERLINGER, POSTFACH 80 13 60, D-81613 MUNCHEN, GERMANY
Language: English Document Type: ARTICLE
Abstract: Effective targeting of short-lived a-emitters such as Bi-213 can be accomplished only with agents that localize rapidly. One such approach uses MAbs that bind to the luminal side of tumor vasculature. MAbs 34A and 201B bind to murine thrombomodulin which is found in lung endothelium. These MAbs were derivatized with CHXb-DTPA and bound Bi-213. The labeled MAbs were shown to deliver over 50% of the injected dose to mouse lungs. The Bi-213 remained in the lungs with a t(1/2) > 4 h, and there was only slight deposition of isotope at other sites (kidney, liver, spleen). Bi-213 coupled to MAb was shown to kill tumor cells in tissue culture efficiently. Injection of large doses (600 mu Ci) of Bi-213 MAb 201 into mice that had previously been injected with EMT-6 tumor cells to form lung colonies resulted in hemorrhage in tumor and normal lung tissue at 4 days post injection. Lower doses (<300 mu Ci/animal) were better tolerated in normal tissue. Successful targeting of Bi-213 to tumor vasculature has been accomplished in this model system and has significant promise for therapy in humans when appropriate targeting reagents are identified.

, **1997**
...Identifiers--MONOCLONAL-ANTIBODY; **TUMOR**-GROWTH; **ALPHA-PARTICLES**; **SOLID** TUMORS; ANGIOGENESIS; INHIBITION; MICE; CELLS; INTERLEUKIN-2; METASTASIS

5/3,K,AB/8 (Item 3 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05157191 Genuine Article#: VD875 Number of References: 33
Title: INDUCTION OF GENOMIC INSTABILITY IN NORMAL HUMAN BRONCHIAL EPITHELIAL-CELLS BY PU-238 **ALPHA-PARTICLES** (Abstract Available)
Author(s): KENNEDY CH; MITCHELL CE; FUKUSHIMA NH; NEFT RE; LECHNER JF
Corporate Source: LOVELACE BIOMED & ENVIRONM RES INST,INHALAT TOXICOL RES INST,POB 5890/ALBUQUERQUE//NM/87185; LOVELACE BIOMED & ENVIRONM RES INST,INHALAT TOXICOL RES INST/ALBUQUERQUE//NM/87185
Journal: CARCINOGENESIS, **1996**, V17, N8 (AUG), P1671-1676
ISSN: 0143-3334
Language: ENGLISH Document Type: ARTICLE
Abstract: Pulmonary deposition of **alpha-particle**-emitting radon daughters is estimated to account for 10% of all lung cancer deaths in the USA, However, the nature and timing of early (preneoplastic) genetic alterations in radon-associated lung cancer are still relatively uncertain, The purpose of this investigation was to determine whether genomic instability occurs after exposure of cultured normal human bronchial epithelial cells to six equal, fractionated doses of a-particles (total doses 2-4 Gy), Two weeks after the final exposure, foci of phenotypically altered cells (PACs) were detected in 0, 63 and 77% of control, low and high dose cultures respectively, Of these, 18% exhibited extended life spans relative to unexposed controls, Elevated frequencies of binucleated cells (BNCs), a marker of genomic instability, were observed in 60 and 38% of the PAC cultures from the low and high dose groups respectively, The micronucleus assay also showed evidence of genomic instability in 40 and 38% of PAC cultures from the low dose and high dose groups respectively, No changes in microsatellite length, another marker of genomic instability, were detected in any of the PAC samples with the 28 markers used for this assay. However, one PAC (L2) showed a hemizygous deletion at 9p13.3. Another PAC (H9), which exhibited the highest frequency of cells containing micronuclei (MN), exhibited a hemizygous deletion at 7q31.3. Each loss may represent a stable mutation that resulted either directly from irradiation or later in progeny of exposed cells because of a-particle-induced genomic instability, The fact that elevated levels of BNCs and MN were present in the progeny many generations after irradiation indicates that the genetic alterations detected with these two markers were not a direct consequence of radiation exposure, but of resulting genomic instability, which may be an early change after exposure to **alpha -particles**.

Title: INDUCTION OF GENOMIC INSTABILITY IN NORMAL HUMAN BRONCHIAL EPITHELIAL-CELLS BY PU-238 **ALPHA-PARTICLES**
, 1996
Abstract: Pulmonary deposition of **alpha-particle**-emitting radon daughters is estimated to account for 10% of all lung cancer deaths in ...

...exposure, but of resulting genomic instability, which may be an early change after exposure to **alpha-particles**.
...Research Fronts: SYNTENY MAPPING)
94-6439 001 (ALL-1 GENE IN ACUTE MYELOID-LEUKEMIA; CLONAL KARYOTYPIC ABNORMALITIES; **CANCER** RISK; CHROMOSOMAL LOCALIZATION; **SOLID** TUMORS)

5/3,K,AB/9 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03374918 Genuine Article#: PB502 Number of References: 41
Title: RADIOIMMUNOTHERAPY OF NUDE-MICE BEARING A HUMAN INTERLEUKIN-2 RECEPTOR ALPHA-EXPRESSING LYMPHOMA UTILIZING THE **ALPHA**-EMITTING **RADIONUCLIDE**-CONJUGATED MONOCLONAL-ANTIBODY BI-212-ANTI-TAC (Abstract Available)
Author(s): HARTMANN F; HORAK EM; GARMESTANI K; WU CC; BRECHBIEL MW; KOZAK RW; TSO J; KOSTEINY SA; GANSOW OA; NELSON DL; WALDMANN TA
Corporate Source: NCI,METAB BRANCH,BLDG 10,ROOM 4N115/BETHESDA//MD/20892; NCI,METAB BRANCH/BETHESDA//MD/20892; NCI,RADIAT ONCOL BRANCH,INORGAN & RADIOIMMUNE CHEM SECT/BETHESDA//MD/20892; US FDA,CTR BIOL EVALUAT & RES,DIV MONOCLONAL ANTIBODIES/BETHESDA//MD/20892; PROT DESIGN LABS INC/MT VIEW//CA/94043
Journal: CANCER RESEARCH, **1994**, V54, N16 (AUG 15), P4362-4370
ISSN: 0008-5472
Language: ENGLISH Document Type: ARTICLE
Abstract: The efficacy, specificity, and toxicity of bismuth (Bi-212) **alpha particle**-mediated **radioimmunotherapy** was evaluated in nude mice bearing a murine lymphoma transfected with the human CD25 [human Tac; interleukin 2 receptor alpha (IL-2R alpha)] gene, The therapeutic agent used was the tumor-specific humanized monoclonal antibody anti-Tac conjugated to Bi-212.

The human IL-2R alpha-expressing cell line was produced by transfecting the gene encoding human Tac into the murine plasmacytoma cell line SP2/0. The resulting cell line, SP2/Tac, expressed approximately 18,000 human IL-2R alpha molecules/cell. Following s.c. or i.p. injection of 2 x 10(6) SP2/Tac cells into nude mice, rapidly growing tumors developed in all animals after a mean of 10 and 13 days, respectively. The bifunctional chelate cyclohexyldiethylenetriaminepentaacetic acid was used to couple Bi-212 to the humanized anti-Tac monoclonal antibody. This immunoconjugate was shown to be stable in vivo. Specifically, in pharmacokinetic studies in nude mice, the blood clearance patterns of i.v. administered Bi-205/206-anti-Tac and coinjected I-125-anti-Tac were comparable. The toxicity and therapeutic efficacy of Bi-212-anti-Tac were evaluated in nude mouse ascites or **solid tumor** models wherein SP2/Tac cells were administered either i.p. or s.c., respectively. The i.p. administration of Bi-212-anti-Tac, 3 days following i.p. tumor inoculation, led to a dose-dependent, significant prolongation of tumor-free survival. Doses of 150 or 200 mu Ci prevented tumor occurrence in 75% (95% confidence interval, 41-93%) of the animals. In the second model, i.v. treatment with Bi-212-anti-Tac 3 days following s.c. tumor inoculation also resulted in a prolongation of the period before tumor development. However, prevention of tumor occurrence decreased to 30% (95% confidence interval, 11-60%). In both the i.p. and s.c. tumor trials, Bi-212-anti-Tac was significantly more effective for i.p. (P2 = 0.0128 50/100 mu Ci Bi-212-anti-Tac versus 50/100 mu Ci Mik beta; P2 = 0.0142 150/200 mu Ci anti-Tac versus 150/200 mu Ci Mik beta) and for s.c. tumors (P2 = 0.0018 100 mu Ci anti-Tac versus 100 mu Ci Mik beta; P2 = 0.0042 200 mu Ci anti-Tac versus 200 mu Ci Mik beta 1) than the control antibody Mik beta 1 coupled to Bi-212 at comparable dose levels. In contrast to the efficacy observed in the adjuvant setting, therapy of large, established s.c. SP-2/ Tac-expressing tumors with i.v. administered Bi-212-anti-Tac (at doses up to 200 mu Ci/animal) failed to induce tumor regression. Pharmacokinetic and tissue distribution studies of radiolabeled anti-Tac in this particular therapeutic situation provided an explanation for this observation. Only 5-6% of the injected dose of radiolabeled antibody was present per g of tumor at 2 h following injection at a time when 75% of the administered Bi-212 radioactivity had decayed. Furthermore, at this time point, there was no greater uptake of Bi-anti-Tac into Tac-expressing tumors than was observed with Tac-nonexpressing variants of SP2/0. Finally, the specific antibody Bi-212/206-anti-Tac was not enriched in the tumor when compared to the irrelevant monoclonal antibody Bi-205/206-Mik beta 1. Although specific enrichment of

radiolabeled Bi-anti-Tac was not seen at 2 h, such enrichment in the tumor was observed at 5 and 24 h postinjection with up to 15.6% injected dose present per g of tumor. The dose limiting acute toxicity following i.v. administration of Bi-212 anti-Tac was bone marrow suppression, which was observed at doses above 200 mu Ci.

In summary, Bi-212-anti-Tac as a complete antibody may be of only limited value in the therapy of bulky solid tumors due to the short physical half-life of Bi-212 and the time required to achieve a useful tumor:normal tissue ratio of the radionuclide following administration of the radiolabeled antibody. However, this radionuclide may be useful in select situations such as adjuvant or intracavitary therapy, strategies that target the vascular endothelial cells of tumors, or in the treatment of leukemias.

Title: RADIOIMMUNOTHERAPY OF NUDE-MICE BEARING A HUMAN INTERLEUKIN-2 RECEPTOR ALPHA-EXPRESSING LYMPHOMA UTILIZING THE **ALPHA**-EMITTING **RADIONUCLIDE**-CONJUGATED MONOCLONAL-ANTIBODY BI-212-ANTI-TAC
, **1994**
Abstract: The efficacy, specificity, and toxicity of bismuth (Bi-212) **alpha particle**-mediated **radioimmunotherapy** was evaluated in nude mice bearing a murine lymphoma transfected with the human CD25 [human...
...and therapeutic efficacy of Bi-212-anti-Tac were evaluated in nude mouse ascites or **solid tumor** models wherein SP2/Tac cells were administered either i.p. or s.c., respectively. The...
Research Fronts: 92-3128 002 (FUNCTIONALIZED AMINO-PHOSPHINIC ACID MACROCYCLIC LIGANDS; **ALPHA-PARTICLE RADIOIMMUNOTHERAPY**; DTPA MONOCLONAL-ANTIBODY CONJUGATES)
92-0689 001 (PSEUDOMONAS EXOTOXIN; INVIVO EFFICACY OF B43 (ANTI-CD19...

5/3,K,AB/10 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03328571 Genuine Article#: NW260 Number of References: 23
Title: RADIOLABELED CHX(B)-2E4 IS STABLE IN-VIVO AND IS A SUITABLE IMMUNOCONJUGATE FOR TESTING **ALPHA-PARTICLE**-EMITTING BISMUTH **RADIONUCLIDES** IN INTERLEUKIN-2 RECEPTOR TARGETED IMMUNOTHERAPY (Abstract Available)
Author(s): TIFFANY LJ; DOBBS D; GARMESTANI K; RAUBITSCHEK A; TINUBU A; BRECHBIEL MW; GOFFMAN T; GANSOW OA; WALDMANN TA; KOZAK RW
Corporate Source: MILES INC,DIV BIOL,4TH & PARKER ST/BERKELEY//CA/94701; US FDA,CTR BIOL EVALUAT & RES,DIV MONOCLONAL ANTIBODIES/BETHESDA//MD/20892 ; NCI,RADIAT ONCOL BRANCH/BETHESDA//MD/20892; NCI,METAB BRANCH/BETHESDA//MD/20892
Journal: ANTIBODY IMMUNOCONJUGATES AND RADIOPHARMACEUTICALS, **1994**, V7 , N2 (SUM), P99-115
ISSN: 0892-7049
Language: ENGLISH Document Type: ARTICLE
Abstract: A murine model system has been established to assess immunotherapeutic approaches to treating interleukin-2 receptor (IL-2R) expressing malignancies. A rat IgG(2c) anti-murine p55 1L-2R monoclonal antibody (2E4) was successfully chelate coupled and radiolabelled with either Indium-lll or Bismuth-206 while retaining full immunoreactivity. The chelating agent used in these studies was p(SCNBZ) CHX(B) DTPA. Indium-111 labeled 2E4 was used to test the in vivo behavior of the immunoconjugate and pre-select murine tumor lines based on in vivo radiolabel uptake. The CHX(B)-2E4 MAb was labelled with either Bismuth-206 or iodine-131 and the two independently radiolabelled antibodies given simultaneously to tumor-bearing nude mice. Both isotopes were found to have equivalent blood clearance and tissue distributions. In addition, 100 percent of the bismuth activity in 1

and 4 hour postinjection serum samples was able to bind to IL-2R expressing cells, while 3 percent bound to an equivalent number of IL-2R negative cells. The time course of in vivo tumor targeting indicated that 25-35 percent of the i.v. injected dose per gram tissue (ID/g) was taken up by a subcutaneous IL-2R positive murine **solid tumor** (EL4J3.4) by 24 h post-injection. In contrast, 8 percent (ID/g) was taken up by the IL-2R receptor negative parental tumor (EL4J). Hence, radiolabeled CHX(B)-2E4 is stable in vivo and is a suitable immunoconjugate for testing **alpha**-emitting bismuth **radionuclides** in anti-IL-2R immunotherapy.

only suitable for testing

Title: RADIOLABELED CHX(B)-2E4 IS STABLE IN-VIVO AND IS A SUITABLE IMMUNOCONJUGATE FOR TESTING **ALPHA-PARTICLE**-EMITTING BISMUTH **RADIONUCLIDES** IN INTERLEUKIN-2 RECEPTOR TARGETED IMMUNOTHERAPY
, **1994**
...Abstract: per gram tissue (ID/g) was taken up by a subcutaneous IL-2R positive murine **solid tumor** (EL4J3.4) by 24 h post-injection. In contrast, 8 percent (ID/g) was taken...

...radiolabeled CHX(B)-2E4 is stable in vivo and is a suitable immunoconjugate for testing **alpha**-emitting bismuth **radionuclides** in anti-IL-2R immunotherapy.
Research Fronts: 92-3128 002 (FUNCTIONALIZED AMINO-PHOSPHINIC ACID MACROCYCLIC LIGANDS; **ALPHA-PARTICLE RADIOIMMUNOTHERAPY**; DTPA MONOCLONAL-ANTIBODY CONJUGATES)

5/3,K,AB/11 (Item 1 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

00677137 Genuine Article#: AG722 Number of References: 14
Title: INVIVO INVESTIGATIONS ON IRRADIATION EFFECTS OF GAMMA-RAYS, FAST-NEUTRONS AND **ALPHA-PARTICLES** FOR A **SOLID** EXPERIMENTAL **TUMOR** (SARCOMA 180) AND IN NORMAL TISSUE - CELL LABELING WITH DEOXYURIDINE-I-125
Author(s): PORSCHEN W; BOSILJANOFF P; MUHLENSIEPEN H; FEINENDEGEN LE
Corporate Source: KERN FORSCH ANLAGE JULICH GMBH/517 JULICH//FEDEP GER/
Journal: ATOMKERNENERGIE, **1975**, V25, N3, P183-189
Language: GERMAN Document Type: ARTICLE

Title: INVIVO INVESTIGATIONS ON IRRADIATION EFFECTS OF GAMMA-RAYS, FAST-NEUTRONS AND **ALPHA-PARTICLES** FOR A **SOLID** EXPERIMENTAL **TUMOR** (SARCOMA 180) AND IN NORMAL TISSUE - CELL LABELING WITH DEOXYURIDINE-I-125
, **1975**
?

Alpha particles are extremely damaging to developing hemopoiesis compared to gamma irradiation.

Jiang TN; Lord BI; Hendry JH

CRC Department of Experimental Haematology, Paterson Institute for Cancer Research, Christie Hospital NHS Trust, Manchester, England.

Radiation research (UNITED STATES) Mar 1994, 137 (3) p380-4, ISSN 0033-7587 Journal Code: QMP

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Estimates of risk of stochastic effects from contamination with **alpha-particle** -emitting radionuclides are based on equivalent doses which take into account the RBE of the high-LET radiation. ICRP has recommended a dose-weighting factor, wR, of 20 for **alpha-particle** radiation. It is assumed that the RBEs for deterministic effects are considerably less than those for stochastic effects. However, the offspring of mice injected with 30 Bq g-1 239Pu at 13 days gestation develop a persistent deficit in hemopoietic stem cells which is primarily the result of damage to their regulatory microenvironment. Their spatial distribution in the marrow is also perturbed, and recent observations on those mice suggested a considerably higher factor than 20. To define a more realistic RBE for hemopoiesis, the effects of external gamma irradiation during the fetal development period have been compared directly with those of 239Pu incorporated via placental transfer on the development of hemopoietic tissue. Pregnant mice were irradiated with 60Co gamma rays (a) continuously from day 13 of gestation to birth at 0.15 or 0.6 Gy/day; (b) six **repeated** acute **doses** (0.6 Gy/min) at 0.1 or 0.3 Gy from day 13 of gestation; (c) one acute dose of 0.6 or 1.8 Gy on day 15 of gestation. The spatial distribution of hemopoietic stem cells in 8-week-old offspring was then determined and compared to that resulting from **alpha-particle** irradiation. In each case, the higher dose was required to match the results for **alpha particles**, suggesting an RBE for developing hemopoiesis of 250-360 compared to a continuous gamma-ray dose and a rather lower value of 130-180 compared to a single acute dose of gamma rays. This contrasts greatly to values for direct irradiation of the stem cells but argues that the effective RBE, measured for long-term effects in vivo, is the more realistic. It is concluded that an all-embracing factor can be grossly misleading in the specification of protection guidelines and can greatly underestimate the risks of exposure to **alpha particles**.

Alpha particles are extremely damaging to developing hemopoiesis compared to gamma irradiation.

Estimates of risk of stochastic effects from contamination with **alpha-particle** -emitting radionuclides are based on equivalent doses which take into account the RBE of the high-LET radiation. ICRP has recommended a dose-weighting factor, wR, of 20 for **alpha-particle** radiation. It is assumed that the RBEs for deterministic effects are considerably less than those...

...13 of gestation to birth at 0.15 or 0.6 Gy/day; (b) six **repeated** acute **doses** (0.6 Gy/min) at 0.1 or 0.3 Gy from day 13 of...

... cells in 8-week-old offspring was then determined and compared to that resulting from **alpha-particle** irradiation. In each case, the higher dose was required to match the results for **alpha particles** , suggesting an RBE for developing hemopoiesis of 250-360 compared to a continuous gamma-ray...

... in the specification of protection guidelines and can greatly underestimate the risks of exposure to **alpha particles**.

Descriptors: **Alpha Particles**; *Gamma Rays; *Hematopoiesis --radiation effects--RE

14/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07793621 92154383 PMID: 1786514
Mechanism of action of platelet activating factor in the pulmonary circulation: an investigation using a novel isotopic system in rabbit isolated lung.
Seale JP; Nourshargh S; Hellewell PG; Williams TJ
Department of Applied Pharmacology, National Heart and Lung Institute, London.

890231 BIOSIS NO.: 199396041732
Zero tumor incidence in mice after repeated lifetime exposures to 0.5 Gy of beta radiation.
AUTHOR: Ootsuyama Akira; Tanooka Hiroshi(a)
AUTHOR ADDRESS: (a)Radiobiol. Div., Natl. Cancer Cent. Res. Inst., Tsukiji, Chuo-ku, Tokyo 104**Japan
JOURNAL: Radiation Research 134 (2):p244-246 1993
ISSN: 0033-7587
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A final series of experiments on tumor induction by repeating 90Sr-90Y beta irradiation of the back of ICR mice three times weekly throughout the life span showed no tumor incidence with **repeated doses** of 0.5 Gy per exposure. The whole **dose**-response relationship for **repeated** irradiation with 0.5 to 11.8 Gy per exposure, summarized along with data obtained previously, showed a unique nonlinear dose response with saturation of tumor incidence at doses of over 2.5 Gy per exposure and a threshold-like value around 1.5 Gy per exposure.

1993

...ABSTRACT: of ICR mice three times weekly throughout the life span showed no tumor incidence with **repeated doses** of 0.5 Gy per exposure. The whole **dose**-response relationship for **repeated** irradiation with 0.5 to 11.8 Gy per exposure, summarized along with data obtained...
MISCELLANEOUS TERMS: ...**ALPHA-PARTICLE** RADIATION

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  File 155:MEDLINE(R)  1966-2002/Apr W2
  File  55:Biosis Previews(R)  1993-2002/Apr W2
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  File  34:SciSearch(R) Cited Ref Sci  1990-2002/Apr W3
        (c) 2002 Inst for Sci Info
  File 434:SciSearch(R) Cited Ref Sci  1974-1989/Dec
        (c) 1998 Inst for Sci Info
  File 340:CLAIMS(R)/US Patent  1950-02/Apr 18
        (c) 2002 IFI/CLAIMS(R)
*File 340: Both the application and grant publication levels for a
patent are in a single record.  See HELP NEWS 340 for details.

      Set  Items  Description
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? s solid(5n)(tumor or cancer or malignan? or carcinoma??)
          584255  SOLID
         1172640  TUMOR
         1064779  CANCER
          453939  MALIGNAN?
          725946  CARCINOMA??
      S1   19622  SOLID(5N)(TUMOR OR CANCER OR MALIGNAN? OR CARCINOMA??)
? s alpha (5n) (isotope or radio?)
>>>File 155 processing for RADIO? stopped at RADIOIMMUNOABSORBENT
>>>File 55 processing for RADIO? stopped at RADIOVISIOGRAPH
>>>File 34 processing for RADIO? stopped at RADIOPHYSICISTS
         1425951  ALPHA
           98883  ISOTOPE
         1218936  RADIO?
      S2    6801  ALPHA (5N) (ISOTOPE OR RADIO?)
? s s1 and s2
           19622  S1
            6801  S2
      S3      11  S1 AND S2
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      S4       9  RD (unique items)
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 4/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12806935   21568783   PMID: 11711678
  Tumor therapy with targeted atomic nanogenerators.
  McDevitt M R; Ma D; Lai L T; Simon J; Borchardt P; Frank R K; Wu K;
Pellegrini V; Curcio M J; Miederer M; Bander N H; Scheinberg D A
  Molecular Pharmacology and Therapeutics Program, Memorial Sloan-Kettering
Cancer Center, 1275 York Avenue, New York, NY 10021, USA.
  Science (United States)  Nov 16 2001,  294  (5546)  p1537-40,  ISSN
0036-8075  Journal Code: 0404511
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Contract/Grant No.: PO1 33049, PHS; RO1 CA55349, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

A single, high linear energy transfer alpha particle can kill a target cell. We have developed methods to target molecular-sized generators of **alpha**-emitting **isotope** cascades to the inside of cancer cells using actinium-225 coupled to internalizing monoclonal antibodies. In vitro, these constructs specifically killed leukemia, lymphoma, breast, ovarian, neuroblastoma, and prostate cancer cells at becquerel (picocurie) levels. Injection of single doses of the constructs at kilobecquerel (nanocurie) levels into mice bearing **solid** prostate **carcinoma** or disseminated human lymphoma induced tumor regression and prolonged survival, without toxicity, in a substantial fraction of animals. Nanogenerators targeting a wide variety of cancers may be possible.

... can kill a target cell. We have developed methods to target molecular-sized generators of **alpha**-emitting **isotope** cascades to the inside of cancer cells using actinium-225 coupled to internalizing monoclonal antibodies...

... levels. Injection of single doses of the constructs at kilobecquerel (nanocurie) levels into mice bearing **solid** prostate **carcinoma** or disseminated human lymphoma induced tumor regression and prolonged survival, without toxicity, in a substantial...

4/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06553268 89092141 PMID: 2910786

The effect of the alpha-emitting radionuclide lead-212 on human ovarian carcinoma: a potential new form of therapy.

Rotmensch J; Atcher RW; Schlenker R; Hines J; Grdina D; Block BS; Press MF; Herbst AL; Weichselbaum RR

Department of Obstetrics and Gynecology, University of Chicago, Pritzker School of Medicine, Illinois 60637.

Gynecologic oncology (UNITED STATES) Feb 1989, 32 (2) p236-9, ISSN 0090-8258 Journal Code: FXC

Contract/Grant No.: 5 RO1 CA-37436, CA, NCI; CA-27476, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

To improve response and survival of patients with ovarian carcinoma noncross-resistant forms of therapy must be developed. alpha-emitting radionuclides may be therapeutically useful since they can directly ionize with energies of 5 to 9 MeV, penetrate only a few cell diameters, and transfer a high amount of energy. The purpose of this study was to determine the effect of the alpha-emitter, lead-212 (212Pb), complexed to sulfur in a nude athymic mouse model (NIH:OVCAR-3) containing human ascites and **solid** epithelial ovarian **carcinoma**. Thirty-six nude mice 28 to 32 days old were injected with 10(7) to 10(8) carcinoma cells from donor mice. After 4 weeks, six groups of six nu/nu athymic BALB-C mice were intraperitoneally injected with 70, 50, 20, 5 microCi of 212Pb sulfur colloid, sulfur colloid, or saline. Tumor necrosis with a decrease in ascites and a dose-related survival were noted with doses of 50, 20, and 5 microCi. With 70 microCi acute gastrointestinal toxicity developed. These experiments form the basis for further investigations and the development of **alpha**-emitting **radiocolloids** which may be of therapeutic efficacy in the treatment of intraperitoneal ovarian carcinoma.

...to sulfur in a nude athymic mouse model (NIH:OVCAR-3) containing human ascites and **solid** epithelial ovarian **carcinoma**. Thirty-six nude mice 28 to 32 days old were injected with 10(7) to...

... gastrointestinal toxicity developed. These experiments form the basis for further investigations and the development of **alpha**-emitting **radiocolloids** which may be of therapeutic efficacy in the treatment of intraperitoneal ovarian carcinoma.

4/3,K,AB/3 (Item 1 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)

12661569 BIOSIS NO.: 200000415071
Delivery of the **alpha**-emitting **radioisotope** bismuth-213 to solid tumors via single-chain Fv and diabody molecules.
AUTHOR: Adams G P(a); Shaller C C; Chappell L L; Wu C; Horak E M; Simmons H H; Litwin S; Marks J D; Weiner L M; Brechbiel M W
AUTHOR ADDRESS: (a)Department of Medical Oncology, Fox Chase Cancer Center, 7701 Burholme Ave., Philadelphia, PA, 19111**USA
JOURNAL: Nuclear Medicine and Biology 27 (4):p339-346 May, 2000
MEDIUM: print
ISSN: 0969-8051
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Intravenously administered anti-tumor single-chain Fv (scFv) and diabody molecules exhibit rapid clearance kinetics and accumulation in tumors that express their cognate antigen. In an attempt to fit the rate of isotope decay to the timing of delivery and duration of tumor retention, anti-HER2/neu CHX-A'' DTPA-C6.5K-A scFv and diabody conjugates were labeled with the alpha-particle emitter 213Bi (t1/2 = 47 min). Radioimmunotherapy studies employing 0.64, 0.35, or 0.15 muCi of 213Bi-labeled C6.5K-A diabody or 1.1, 0.6, or 0.3 muCi of 213Bi-labeled C6.5K-A scFv were performed in nude mice bearing early, established SK-OV-3 tumors. Only the 0.3 muCi dose of 213Bi-labeled C6.5K-A scFv resulted in both acceptable toxicity and a reduction in tumor growth rate. The specificity of the anti-tumor effects was determined by comparing the efficacy of treatment with 0.3 and 0.15 muCi doses of 213Bi-labeled C6.5K-A scFv and 213Bi-labeled NM3E2 (an irrelevant scFv) in nude mice bearing large established tumors. The 0.3 muCi dose of 213Bi on both the C6.5K-A and NM3E2 scFvs resulted in similar anti-tumor effects (p = 0.46) indicating that antigen-specific targeting was not a factor. This suggests that the physical half-life of 213Bi may be too brief to be effectively paired with systemically-administered diabody or scFv molecules.

2000

Delivery of the **alpha**-emitting **radioisotope** bismuth-213 to solid tumors via single-chain Fv and diabody molecules.
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: ...**alpha**-emitting **radioisotope**, **solid tumor** delivery

4/3,K,AB/4 (Item 2 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)

09443625 BIOSIS NO.: 199497451995
Radioimmunotherapy of nude mice bearing a human interleukin 2 receptor alpha-expressing lymphoma utilizing the **alpha**-emitting **radionuclide**-conjugated monoclonal antibody 212Bi-anti-Tac.

AUTHOR: Hartmann Frank; Horak Eva M; Garmestani Kayhan; Wu Chuanchu; Brechbiel Martin W; Kozak Robert W; Tso J; Kosteiny Sheri A; Gansow Otto A; Nelson David L; Waldmann Thomas A(a)
AUTHOR ADDRESS: (a)Metabolic Branch, Natl. Cancer Inst., Build. 10, 4N115, NIH, Bethesda, MD 20892**USA
JOURNAL: Cancer Research 54 (16):p4362-4370 1994
ISSN: 0008-5472
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The efficacy, specificity, and toxicity of bismuth (212Bi) **alpha** particle-mediated **radioimmunotherapy** was evaluated in nude mice bearing a murine lymphoma transfected with the human CD25 (human Tac; interleukin 2 receptor alpha (IL-2R-alpha)) gene. The therapeutic agent used was the tumor-specific humanized monoclonal antibody anti-Tac conjugated to 212Bi. The human IL-2R-alpha-expressing cell line was produced by transfecting the gene encoding human Tac into the murine plasmacytoma cell line SP2/0. The resulting cell line, SP2/Tac, expressed approximately 18,000 human IL-2R-alpha molecules/cell. Following s.c. or i.p. injection of 2 times 10-6 SP2/Tac cells into nude mice, rapidly growing tumors developed in all animals after a mean of 10 and 13 days, respectively. The bifunctional chelate cyclohexyldiethylenetriaminepentaacetic acid was used to couple 212Bi to the humanized anti-Tac monoclonal antibody. This immunoconjugate was shown to be stable in vivo. Specifically, in pharmacokinetic studies in nude mice, the blood clearance patterns of i.v. administered 205/206Bi-anti-Tac and coinjected 125I-anti-Tac were comparable. The toxicity and therapeutic efficacy of 212Bi-anti-Tac were evaluated in nude mouse ascites or **solid tumor** models wherein SP2/Tac cells were administered either i.p. or s.c., respectively. The i.p. administration of 212Bi-antiTac, 3 days following i.p. tumor inoculation, led to a dose-dependent, significant prolongation of tumor-free survival. Doses of 150 or 200 mu-Ci prevented tumor occurrence in 75% (95% confidence interval, 41-93%) of the animals. In the second model, i.v. treatment with 212Bi-anti-Tac 3 days following s.c. tumor inoculation also resulted in a prolongation of the period before tumor development. However, prevention of tumor occurrence decreased to 30% (95% confidence interval, 11-60%). In both the i.p. and s.c. tumor trials, 212Bi-anti-Tac was significantly more effective for i.p. (P2 = 0.0128 50/100 mu-Ci 212Bi-anti-Tac versus 50/100 mu-Ci Mik-beta; P2 = 0.0142 150/200 mu-Ci anti-Tac versus 150/200 mu-Ci Mik-beta) and for s.c. tumors (P2 = 0.0018 100,uCi anti-Tac versus 100 mu-Ci Mik-beta; P2 = 0.0042 200 mu-Ci anti-Tac versus 200 mu-Ci Mik-beta-1) than the control antibody Mik/beta-1 coupled to 212Bi at comparable dose levels. In contrast to the efficacy observed in the adjuvant setting, therapy of large, established s.c. SP-2/ Tac-expressing tumors with i.v. administered 212Bi-anti-Tac (at doses up to 200 mu-Ci/animal) failed to induce tumor regression. Pharmacokinetic and tissue distribution studies of radiolabeled anti-Tac in this particular therapeutic situation provided an explanation for this observation. Only 5-6% of the injected dose of radiolabeled antibody was present per g o tumor at 2 h following injection at a time when 75% of the administered 212Bi radioactivity had decayed. Furthermore, at this time point, there was no greater uptake of Bi-anti-Tac into Tac-expressing tumors than wa observed with Tac-nonexpressing variants of SP2/0. Finally, the specific antibody 205/206Bi-anti-Tac was not enriched in the tumor when compare to the irrelevant monoclonal antibody 205/206Bi-Mik-beta-1. Although specific enrichment of radiolabeled Bi-anti-Tac was not seen at 2 h, such enrichment in the tumor was observed at 5 and 24 h postinjection with up to 15.6% injected dose present per g of tumor. The dose-limiting acute toxicity following i.v. administration of 212Bi-anti-Tac was bone marrow suppression, which was observed at doses above 200 mu-Ci. In summary, 212Bi-anti-Tac as a complete antibody may be of only limited value in the therapy of bulky

solid tumors due to the short physical half-life of 212Bi and the time required to achieve a useful tumor:normal tissue ratio of the radionuclide following administration of the radiolabeled antibody. However, this radionuclide may be useful in select situations such as adjuvant or intracavitary therapy, strategies that target the vascular endothelial cells of tumors, or in the treatment of leukemias.

1994

Radioimmunotherapy of nude mice bearing a human interleukin 2 receptor alpha-expressing lymphoma utilizing the **alpha**-emitting **radionuclide**-conjugated monoclonal antibody 212Bi-anti-Tac.

ABSTRACT: The efficacy, specificity, and toxicity of bismuth (212Bi) **alpha** particle-mediated **radioimmunotherapy** was evaluated in nude mice bearing a murine lymphoma transfected with the human CD25 (human...

...toxicity and therapeutic efficacy of 212Bi-anti-Tac were evaluated in nude mouse ascites or **solid tumor** models wherein SP2/Tac cells were administered either i.p. or s.c., respectively. The...

4/3,K,AB/5 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

10030457 Genuine Article#: 475QJ Number of References: 31
Title: Theoretical estimation of absorbed dose to organs in radioimmunotherapy using radionuclides with multiple unstable daughters (ABSTRACT AVAILABLE)
Author(s): Hamacher KA (REPRINT) ; Sgouros G
Corporate Source: Cornell Univ,New York Presbyterian Hosp, Weill Med Coll,525 E 68th St/New York//NY/10021 (REPRINT); Mem Sloan Kettering Canc Ctr,New York//NY/10021
Journal: MEDICAL PHYSICS, 2001, V28, N9 (SEP), P1857-1874
ISSN: 0094-2405 Publication date: 20010900
Publisher: AMER INST PHYSICS, CIRCULATION & FULFILLMENT DIV, 2 HUNTINGTON QUADRANGLE, STE 1 N O 1, MELVILLE, NY 11747-4501 USA
Language: English Document Type: ARTICLE
Abstract: The toxicity and clinical utility of long-lived alpha emitters such as Ac-225 and Ra-223 will depend upon the fate of alpha-particle emitting unstable intermediates generated after decay of the conjugated parent. For example, decay of Ac-225 to a stable element yields four **alpha** particles and seven **radionuclides**. Each of these progeny has its own free-state biodistribution and characteristic half-life. Therefore, their inclusion for a more accurate prediction of absorbed dose and potential toxicity requires a formalism that takes these factors into consideration as well. To facilitate the incorporation of such intermediates into the dose calculation, a previously developed methodology (model 1) has been extended. Two new models (models 2 and 3) for allocation of daughter products are introduced and are compared with the previously developed model. Model I restricts the transport to a function that yields either the place of origin or the place(s) of biodistribution depending on the half-life of the parent radionuclide. Model 2 includes the transient time within the bloodstream and model 3 incorporates additional binding at or within the tumor. This means that model 2 also allows for radionuclide decay and further daughter production while moving from one location to the next and that model 3 relaxes the constraint that the residence time within the tumor is solely based on the half-life of the parent. The models are used to estimate normal organ absorbed doses for the following parent radionuclides: Ac-225, Pb-212, At-211, Ra-223, and Bi-213. Model simulations are for a 0.1 g rapidly accessible

tumor and a 10 g **solid tumor**. Additionally, the effects of varying radiolabled carrier molecule purity and amount of carrier molecules, as well as tumor cell antigen saturation are examined. The results indicate that there is a distinct advantage in using parent radionuclides such as Ac-225 or Ra-223, each having a half-life of more than 10 days and yielding four alpha particles per parent decay, in that lower doses to normal organs result for a given tumor dose in comparison to those **radionuclides** yielding fewer **alpha** particles. In model 2, which accounts for transit time through the blood, a dose of 20 Gy to a rapidly accessible 0. 1 g tumor will result in a liver and kidney dose of 1.7 and 0.9 Gy, respectively from Ac-225. An equivalent dose to tumor from Ra-223 would yield a maximum normal organ dose of 0.4 and 0.3 Gy to bone and small intestines, respectively; the corresponding absorbed dose to small intestines from Pb-212 and Bi-213 is 2.2 and 3.0 Gy, respectively. (C) 2001 American Association of Physicists in Medicine.

...Abstract: the conjugated parent. For example, decay of Ac-225 to a stable element yields four **alpha** particles and seven **radionuclides**. Each of these progeny has its own free-state biodistribution and characteristic half-life. Therefore...

...Ra-223, and Bi-213. Model simulations are for a 0.1 g rapidly accessible **tumor** and a 10 g **solid tumor**. Additionally, the effects of varying radiolabled carrier molecule purity and amount of carrier molecules, as...

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4/3,K,AB/6 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06616100 Genuine Article#: ZE898 Number of References: 29
Title: Vascular targeted **radioimmunotherapy** with Bi-213 - An **alpha**-particle emitter (ABSTRACT AVAILABLE)
Author(s): Kennel SJ (REPRINT) ; Mirzadeh S
Corporate Source: OAK RIDGE NATL LAB,DIV LIFE SCI, POB 2009/OAK RIDGE//TN/37831 (REPRINT)
Journal: NUCLEAR MEDICINE AND BIOLOGY, 1998, V25, N3 (APR), P241-246
ISSN: 0969-8051 Publication date: 19980400
Publisher: ELSEVIER SCIENCE INC, 655 AVENUE OF THE AMERICAS, NEW YORK, NY 10010
Language: English Document Type: ARTICLE
Abstract: To destroy both tumor blood vessels and adjacent tumor cells, an cu particle emitter, Bi-213, has been targeted with a monoclonal antibody (MAb) to vessels that feed lung tumors in mice. Animals, bearing approximately 100 EMT-6 carcinomas each of 50-400 cells in size in the lung, that were treated with 120 mu Ci of Bi-213-MAb 201B were all cured of their disease, Animals treated when tumors were larger (10(3)-10(4) cells) had extended life spans, but a small number of residual tumors eventually killed the animals. Significant extension of life span was also induced with another tumor model - rat tracheal carcinoma growing in the lungs of SCID mice that were then treated with 136 mu Ci Bi-213-MAb B-201. These studies indicate that attack of both blood vessels and tumor cells simultaneously is an effective mode of cancer treatment. (C) 1998 Elsevier Science Inc.

Title: Vascular targeted **radioimmunotherapy** with Bi-213 - An **alpha**-particle emitter

...Identifiers--MONOCLONAL-ANTIBODIES; **TUMOR**-GROWTH; ENDOTHELIAL-CELLS; EPITHELIAL-CELLS; **SOLID** TUMORS; INHIBITION; ANGIOGENESIS; THERAPY; METASTASIS; INVIVO

4/3,K,AB/7 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06394337 Genuine Article#: YP202 Number of References: 37
Title: Radioimmunotherapy targeting of HER2/neu oncoprotein on ovarian tumor using lead-212-DOTA-AE1 (ABSTRACT AVAILABLE)
Author(s): Horak E; Hartmann F; Garmestani K; Wu CC; Brechbiel M; Gansow OA ; Landolfi NF; Waldmann TA (REPRINT)
Corporate Source: NCI,METAB BRANCH, NIH, BLDG 10, ROOM 4N115/BETHESDA//MD/20892 (REPRINT); NCI,METAB BRANCH, NIH/BETHESDA//MD/20892; NCI,INORGAN & RADIOIMMUNE CHEM SECT, RADIAT ONCOL BRANCH, NIH/BETHESDA//MD/20892; PROT DESIGN LABS INC,/MT VIEW//CA/
Journal: JOURNAL OF NUCLEAR MEDICINE, 1997, V38, N12 (DEC), P1944-1950
ISSN: 0161-5505 Publication date: 19971200
Publisher: SOC NUCLEAR MEDICINE INC, 1850 SAMUEL MORSE DR, RESTON, VA 20190-5316
Language: English Document Type: ARTICLE
Abstract: The specificity, toxicity and efficacy of lead (Pb-212) radioimmunotherapy were evaluated in nude mice bearing the SK-OV-3 human ovarian tumor cell line expressing the HER2/neu proto-oncogene. Methods: The therapeutic agent used was the tumor-specific anti-HER2/neu monoclonal antibody AE1 conjugated to Pb-212, Bi-212 being the daughter and thus the source of the alpha-particle and beta emissions. A bifunctional derivative of tetraazacyclododecanetetraacetic acid (p-SCN-Bz-DOTA) was used to couple Pb-212 to the anti-HER2/neu monoclonal antibody AE1. The chelating agent did not alter the binding affinity to its antigenic target or the pharmacokinetics and tissue distribution of the AE1 antibody, Toxicity and therapeutic efficacy of Pb-212-AE1 were evaluated in nude mouse ascites or **solid tumor** models, wherein SK-OV-3 cells were administered i.p. or s.c., respectively. Results: The dose-limiting acute toxicity after i.v. administration of Pb-212-AE1 was bone marrow suppression, which was observed at doses above 25 mu Ci. Therefore, doses of 10 and 20 mu Ci were used in efficacy trials. The i.p. administration of Pb-212-AE1 3 days after i.p. tumor inoculation led to a significant (p(2) = 0.015) prolongation of tumor-free survival. In a second model, i.v. treatment with Pb-212-AE1 3 days after s.c. tumor inoculation prevented subsequent tumor development in all animals treated with 10 or 20 mu Ci of Pb-212-AE1 (p(2) = 0.002 compared to control groups). This efficacy in the adjuvant setting was antibody specific because treatments with equivalently labeled control antibody or unlabeled AE1 antibody or no treatment were less effective. The rate of growth of small (mean tumor volume, 15 mm(3)) SK-OV-3 tumors was modestly inhibited. However, tumor growth was not inhibited in mice bearing larger (mean tumor volume, 146 mm(3)) SK-OV-3 tumors by the administration of a single dose of 10 or 20 mu Ci of Pb-212-AE1. Conclusion: Lead-212-AE1 as an intact radiolabeled monoclonal antibody may be of only modest value in the therapy of bulky solid tumors due to the short physical half-life of Pb-212 and time required to achieve a useful tumor-to-normal tissue ratio of radionuclide after administration. However, the radiolabeled monoclonal antibody may be useful in therapy of tumors in the adjuvant setting. Furthermore, Pb-212 may be of value in select situations, including treatment of leukemia, intercavitary therapy or strategies that target vascular endothelial cells of tumors.

...Abstract: Toxicity and therapeutic efficacy of Pb-212-AE1 were evaluated

in nude mouse ascites or **solid tumor** models, wherein SK-OV-3 cells were administered i.p. or s.c., respectively. Results...

4/3,K,AB/8 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03374918 Genuine Article#: PB502 Number of References: 41
Title: RADIOIMMUNOTHERAPY OF NUDE-MICE BEARING A HUMAN INTERLEUKIN-2 RECEPTOR ALPHA-EXPRESSING LYMPHOMA UTILIZING THE **ALPHA**-EMITTING **RADIONUCLIDE**-CONJUGATED MONOCLONAL-ANTIBODY BI-212-ANTI-TAC (Abstract Available)
Author(s): HARTMANN F; HORAK EM; GARMESTANI K; WU CC; BRECHBIEL MW; KOZAK RW; TSO J; KOSTEINY SA; GANSOW OA; NELSON DL; WALDMANN TA
Corporate Source: NCI,METAB BRANCH,BLDG 10,ROOM 4N115/BETHESDA//MD/20892; NCI,METAB BRANCH/BETHESDA//MD/20892; NCI,RADIAT ONCOL BRANCH,INORGAN & RADIOIMMUNE CHEM SECT/BETHESDA//MD/20892; US FDA,CTR BIOL EVALUAT & RES,DIV MONOCLONAL ANTIBODIES/BETHESDA//MD/20892; PROT DESIGN LABS INC/MT VIEW//CA/94043
Journal: CANCER RESEARCH, 1994, V54, N16 (AUG 15), P4362-4370
ISSN: 0008-5472
Language: ENGLISH Document Type: ARTICLE
Abstract: The efficacy, specificity, and toxicity of bismuth (Bi-212) **alpha** particle-mediated **radioimmunotherapy** was evaluated in nude mice bearing a murine lymphoma transfected with the human CD25 [human Tac; interleukin 2 receptor alpha (IL-2R alpha)] gene, The therapeutic agent used was the tumor-specific humanized monoclonal antibody anti-Tac conjugated to Bi-212.

The human IL-2R alpha-expressing cell line was produced by transfecting the gene encoding human Tac into the murine plasmacytoma cell line SP2/0. The resulting cell line, SP2/Tac, expressed approximately 18,000 human IL-2R alpha molecules/cell. Following s.c. or i.p. injection of 2 x 10(6) SP2/Tac cells into nude mice, rapidly growing tumors developed in all animals after a mean of 10 and 13 days, respectively. The bifunctional chelate cyclohexyldiethylenetriaminepentaacetic acid was used to couple Bi-212 to the humanized anti-Tac monoclonal antibody. This immunoconjugate was shown to be stable in vivo. Specifically, in pharmacokinetic studies in nude mice, the blood clearance patterns of i.v. administered Bi-205/206-anti-Tac and coinjected I-125-anti-Tac were comparable. The toxicity and therapeutic efficacy of Bi-212-anti-Tac were evaluated in nude mouse ascites or **solid tumor** models wherein SP2/Tac cells were administered either i.p. or s.c., respectively. The i.p. administration of Bi-212-anti-Tac, 3 days following i.p. tumor inoculation, led to a dose-dependent, significant prolongation of tumor-free survival. Doses of 150 or 200 mu Ci prevented tumor occurrence in 75% (95% confidence interval, 41-93%) of the animals. In the second model, i.v. treatment with Bi-212-anti-Tac 3 days following s.c. tumor inoculation also resulted in a prolongation of the period before tumor development. However, prevention of tumor occurrence decreased to 30% (95% confidence interval, 11-60%). In both the i.p. and s.c. tumor trials, Bi-212-anti-Tac was significantly more effective for i.p. (P2 = 0.0128 50/100 mu Ci Bi-212-anti-Tac versus 50/100 mu Ci Mik beta; P2 = 0.0142 150/200 mu Ci anti-Tac versus 150/200 mu Ci Mik beta) and for s.c. tumors (P2 = 0.0018 100 mu Ci anti-Tac versus 100 mu Ci Mik beta; P2 = 0.0042 200 mu Ci anti-Tac versus 200 mu Ci Mik beta 1) than the control antibody Mik beta 1 coupled to Bi-212 at comparable dose levels. In contrast to the efficacy observed in the adjuvant setting, therapy of large, established s.c. SP-2/ Tac-expressing tumors with i.v. administered Bi-212-anti-Tac (at doses up to 200 mu Ci/animal) failed to induce tumor regression. Pharmacokinetic and tissue distribution studies of radiolabeled anti-Tac in this particular therapeutic situation provided an explanation for this observation.

Only 5-6% of the injected dose of radiolabeled antibody was present per g of tumor at 2 h following injection at a time when 75% of the administered Bi-212 radioactivity had decayed. Furthermore, at this time point, there was no greater uptake of Bi-anti-Tac into Tac-expressing tumors than was observed with Tac-nonexpressing variants of SP2/0. Finally, the specific antibody Bi-212/206-anti-Tac was not enriched in the tumor when compared to the irrelevant monoclonal antibody Bi-205/206-Mik beta 1. Although specific enrichment of radiolabeled Bi-anti-Tac was not seen at 2 h, such enrichment in the tumor was observed at 5 and 24 h postinjection with up to 15.6% injected dose present per g of tumor. The dose limiting acute toxicity following i.v. administration of Bi-212 anti-Tac was bone marrow suppression, which was observed at doses above 200 mu Ci.

In summary, Bi-212-anti-Tac as a complete antibody may be of only limited value in the therapy of bulky solid tumors due to the short physical half-life of Bi-212 and the time required to achieve a useful tumor:normal tissue ratio of the radionuclide following administration of the radiolabeled antibody. However, this radionuclide may be useful in select situations such as adjuvant or intracavitary therapy, strategies that target the vascular endothelial cells of tumors, or in the treatment of leukemias.

Title: RADIOIMMUNOTHERAPY OF NUDE-MICE BEARING A HUMAN INTERLEUKIN-2 RECEPTOR ALPHA-EXPRESSING LYMPHOMA UTILIZING THE **ALPHA**-EMITTING **RADIONUCLIDE**-CONJUGATED MONOCLONAL-ANTIBODY BI-212-ANTI-TAC
Abstract: The efficacy, specificity, and toxicity of bismuth (Bi-212) **alpha** particle-mediated **radioimmunotherapy** was evaluated in nude mice bearing a murine lymphoma transfected with the human CD25 [human...
...and therapeutic efficacy of Bi-212-anti-Tac were evaluated in nude mouse ascites or **solid tumor** models wherein SP2/Tac cells were administered either i.p. or s.c., respectively. The...
Research Fronts: 92-3128 002 (FUNCTIONALIZED AMINO-PHOSPHINIC ACID MACROCYCLIC LIGANDS; **ALPHA**-PARTICLE **RADIOIMMUNOTHERAPY**; DTPA MONOCLONAL-ANTIBODY CONJUGATES)
92-0689 001 (PSEUDOMONAS EXOTOXIN; INVIVO EFFICACY OF B43 (ANTI-CD19...

4/3,K,AB/9 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03328571 Genuine Article#: NW260 Number of References: 23
Title: RADIOLABELED CHX(B)-2E4 IS STABLE IN-VIVO AND IS A SUITABLE IMMUNOCONJUGATE FOR TESTING **ALPHA**-PARTICLE-EMITTING BISMUTH **RADIONUCLIDES** IN INTERLEUKIN-2 RECEPTOR TARGETED IMMUNOTHERAPY (Abstract Available)
Author(s): TIFFANY LJ; DOBBS D; GARMESTANI K; RAUBITSCHEK A; TINUBU A; BRECHBIEL MW; GOFFMAN T; GANSOW OA; WALDMANN TA; KOZAK RW
Corporate Source: MILES INC,DIV BIOL,4TH & PARKER ST/BERKELEY//CA/94701; US FDA,CTR BIOL EVALUAT & RES,DIV MONOCLONAL ANTIBODIES/BETHESDA//MD/20892 ; NCI,RADIAT ONCOL BRANCH/BETHESDA//MD/20892; NCI,METAB BRANCH/BETHESDA//MD/20892
Journal: ANTIBODY IMMUNOCONJUGATES AND RADIOPHARMACEUTICALS, 1994, V7, N2 (SUM), P99-115
ISSN: 0892-7049
Language: ENGLISH Document Type: ARTICLE
Abstract: A murine model system has been established to assess immunotherapeutic approaches to treating interleukin-2 receptor (IL-2R) expressing malignancies. A rat IgG(2c) anti-murine p55 1L-2R monoclonal antibody (2E4) was successfully chelate coupled and radiolabelled with either Indium-111 or Bismuth-206 while retaining full immunoreactivity. The chelating agent used in these studies was p(SCNBZ) CHX(B) DTPA.

Indium-111 labeled 2E4 was used to test the in vivo behavior of the immunoconjugate and pre-select murine tumor lines based on in vivo radiolabel uptake. The CHX(B)-2E4 MAb was labelled with either Bismuth-206 or iodine-131 and the two independently radiolabelled antibodies given simultaneously to tumor-bearing nude mice. Both isotopes were found to have equivalent blood clearance and tissue distributions. In addition, 100 percent of the bismuth activity in 1 and 4 hour postinjection serum samples was able to bind to IL-2R expressing cells, while 3 percent bound to an equivalent number of IL-2R negative cells. The time course of in vivo tumor targeting indicated that 25-35 percent of the i.v. injected dose per gram tissue (ID/g) was taken up by a subcutaneous IL-2R positive murine **solid tumor** (EL4J3.4) by 24 h post-injection. In contrast, 8 percent (ID/g) was taken up by the IL-2R receptor negative parental tumor (EL4J). Hence, radiolabeled CHX(B)-2E4 is stable in vivo and is a suitable immunoconjugate for testing **alpha**-emitting bismuth **radionuclides** in anti-IL-2R immunotherapy.

Title: RADIOLABELED CHX(B)-2E4 IS STABLE IN-VIVO AND IS A SUITABLE IMMUNOCONJUGATE FOR TESTING **ALPHA**-PARTICLE-EMITTING BISMUTH **RADIONUCLIDES** IN INTERLEUKIN-2 RECEPTOR TARGETED IMMUNOTHERAPY

...Abstract: per gram tissue (ID/g) was taken up by a subcutaneous IL-2R positive murine **solid tumor** (EL4J3.4) by 24 h post-injection. In contrast, 8 percent (ID/g) was taken...

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Research Fronts: 92-3128 002 (FUNCTIONALIZED AMINO-PHOSPHINIC ACID MACROCYCLIC LIGANDS; **ALPHA**-PARTICLE **RADIOIMMUNOTHERAPY**; DTPA MONOCLONAL-ANTIBODY CONJUGATES)

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Set     Items   Description
S1    1425951   ALPHA
S2    2419044   TUMOR OR CANCER OR MALIGNAN? OR CARCINOMA??
S3     234429   S1 AND S2
S4      23538   REPEAT? (5N) (INJECT? OR DOSE?? OR DOSAGE?? OR ADMINISTER?)
S5        514   S3 AND S4
S6    1296548   ANTIBOD?
S7        108   S5 AND S6
S8     584255   SOLID
S9          0   S7 AND S8
S10        19   S5 AND S8
S11        12   RD (unique items)
S12     19563   ALPHA (5N) (PARTICLE?? OR ISOTOPE OR RADIOLABEL? OR RADIO?)
S13        13   S12 AND S4
S14        11   RD (unique items)
? s repeat?
     S15  547880  REPEAT?
? s s2 and s12
          2419044  S2
            19563  S12
     S16    2175  S2 AND S12
? s s16 and s15
             2175  S16
           547880  S15
     S17      43  S16 AND S15
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S18      32  RD (unique items)
? s s18 and py<=1998
Processing
Processing
               32  S18
         33496514  PY<=1998
     S19      20  S18 AND PY<=1998
? s s19 and antibod?
               20  S19
          1296548  ANTIBOD?
     S20       2  S19 AND ANTIBOD?
? t s20/3,k,ab/1-2

 20/3,K,AB/1     (Item 1 from file: 34)
DIALOG(R)File  34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

00929092   Genuine Article#: FH117   Number of References: 35
Title: MONITORING OF SERUM ALPHA-FETOPROTEIN LEVELS IN CHILDREN WITH
    CHRONIC HEPATITIS-B VIRUS-INFECTION  (Abstract Available)
Author(s): VAJRO P; FONTANELLA A; DEVINCENZO A; LETTERA P; GRECO L; COPPA A
    ; DARMIENTO M
Corporate Source: UNIV NAPLES SCH MED,DEPT PEDIAT,VIA S PANSINI 5/I-80131
    NAPLES//ITALY/; UNIV NAPLES SCH MED,DEPT CLIN PATHOL/I-80131
    NAPLES//ITALY/; UNIV NAPLES SCH MED,DEPT PATHOL/I-80131 NAPLES//ITALY/
Journal: JOURNAL OF PEDIATRIC GASTROENTEROLOGY AND NUTRITION, 1991, V
    12, N1, P27-32
Language: ENGLISH   Document Type: ARTICLE
Abstract: Changes in serum alpha-fetoprotein (alpha-FP) levels were
    investigated by radioimmunoassay during the follow-up (17 +/- 12
    months, two to three times per year) of 50 children with chronic
    hepatitis B virus infection (mean age of 8 years, 30 males) and of 35
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healthy age- and sex-matched controls. Eleven of 50 were healthy carriers; 7 had chronic persistent hepatitis, 29 had chronic active hepatitis, and 3 had cirrhosis-associated chronic active hepatitis. Serum alpha-FP levels in controls were found to be always lower than 5 ng/ml (0.1-4.4 ng/ml, xBAR +/- SD of 1.34 +/- 1.32 ng/ml). Statistical analysis after logarithmic transformation showed a significant difference between mean levels (ng/ml) in controls and in patients [geometric mean = 0.83 C.L. (95% confidence limits of 1.19/0.58) vs. 3.43 (95% C.L. of 4.79/2.45); p = 0.0001]. Mean values of serum alpha-FP levels at entry were higher than those found at the end of the follow-up period [geometric mean = 3 (95% C.L. of 4.69/1.92) vs. 1.48 (95% C.L. of 2.13/0.95); p = 0.038]. Only three patients **repeatedly** showed high alpha-FP levels (76.7, 122.8, and 1,600 ng/ml at entry): alpha-FP values became normal after a mean follow-up of 17 +/- 7.8 months as well as liver enzymes, with no changes in serum "e" antigen-**antibody** and anti-delta **antibody** status being observed. Mean values of serum alpha-FP levels in HBeAg-positive patients were significantly higher than in HBeAg-negative patients both at entry and during the follow-up (p = 0.05). Serum logarithmic alpha-FP values were significantly correlated with log aminotransferases (alanine aminotransferase: r = 0.38 and p < 0.0001; aspartate aminotransferase: r = 0.36 and p < 0.0001) and log gamma-glutamyl transpeptidase (r = 0.32 and p < 0.0001). Although serum alpha-FP levels were found to be higher in patients with the most severe histological damage, they did not allow the accurate discrimination of histological categories in individual patients.

, **1991**
Abstract: Changes in serum alpha-fetoprotein (**alpha**-FP) levels were investigated by **radioimmunoassay** during the follow-up (17 +/- 12 months, two to three times per year) of 50...

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...7.8 months as well as liver enzymes, with no changes in serum "e" antigen-**antibody** and anti-delta **antibody** status being observed. Mean values of serum alpha-FP levels in HBeAg-positive patients were...
...Identifiers--CHRONIC ACTIVE-HEPATITIS; CHRONIC LIVER-DISEASE; HEPATOCELLULAR-**CARCINOMA**; VIRAL-HEPATITIS; SURFACE-ANTIGEN; NORMAL INFANTS; RADIOIMMUNOASSAY; REGENERATION; CIRRHOSIS; NECROSIS

20/3,K,AB/2 (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 1766592 IFI Acc No: 8708997 IFI Acc No: 2726953
Document Type: CM
COMPOSITION AND METHOD FOR DETECTING AND TREATING **CANCER**
Inventors: LEMELSON JEROME H (US)
Assignee: UNASSIGNED OR ASSIGNED TO INDIVIDUAL
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 4665897 **19870519** US 84614038 19840525
Publication Kind: A
Calculated Expiration: 20040525
(Cited in 008 later patents)
Priority Applic(No,Date): US 84614038 19840525

Abstract: Improvements in methods for treating diseases and tumors with compositions of matter defining drug units, each of which includes an

antibody, such as a monoclonal **antibody** produced outside of the body of a living being to be treated. Each unit contains a quantity of normally inactive nuclide capable of being rendered radioactive for treating a disease and a quantity of a second nuclide which may be normally inactive or radioactive, such as a radionuclide. The **antibody** is targeted to a specific antigen existing in the patient being treated. The drug units emit such radiation upon being activated within the body by radiation such as neutron radiation generated to detect the presence of a particular disease in a living being and to provide an indication of the location and extent of such disease. Once a concentration of disease cells is so located by analyzing signals derived from one or more detectors of radiation generated by a nuclide carried by **antibodies** to the disease site, and its extent or shape is determined by analysis of direct or reconstructed images of the interior of the body at the site, nuclide material carried to the detected site may be activated by properly controlling the location of a source of activating radiation, its direction and activation to effect treatment of the disease. Treatment radiation may include atomic disintegration of a small quantity of a nuclide, such as boron-10 by absorption of neutrons directed through the body, which disintegration results in the generation of high velocity particles or fragments capable of the localized destruction of diseased cells such as **cancer** cells.

COMPOSITION AND METHOD FOR DETECTING AND TREATING **CANCER**
Publication (No,Date), Applic (No,Date):
...**19870519**
Abstract: ...diseases and tumors with compositions of matter defining drug units, each of which includes an **antibody**, such as a monoclonal **antibody** produced outside of the body of a living being to be treated. Each unit contains...

...a second nuclide which may be normally inactive or radioactive, such as a radionuclide. The **antibody** is targeted to a specific antigen existing in the patient being treated. The drug units...

...signals derived from one or more detectors of radiation generated by a nuclide carried by **antibodies** to the disease site, and its extent or shape is determined by analysis of direct...

...high velocity particles or fragments capable of the localized destruction of diseased cells such as **cancer** cells.

Exemplary Claim: ...MATTER COMPRISING IN COMBINATION (A) A MULTITUDE OF DRUG UNITS, EACH UNIT DEFINED BY A **ANTIBODY** TARGETED TO A SPECIFIC ANTIGEN IN A LIVING BEING, AND A FIRST QUANTITY OF A FIRST NORMALLY INACTIVE NUCLIDE INTEGRALLY SECURED TO SAID **ANTIBODY**, (B) SAID FIRST QUANTITY OF SAID FIRST NUCLIDE BEING CAPABLE OF BEING RENDERED RADIOACTIVE WHEN...
Non-exemplary Claims: ...miniature fat globule containing said quantities of said first and second nuclides and supporting said **antibody**.
...

...13. A composition of matter in accordance with claim 1 wherein said **antibody** and said first and second nuclides are incorporated into said **antibody** by a derivatizing agent which is selected from the group of polymers which include esters...

...14. A composition of matter in accordance with claim 1 wherein said **antibody** and said nuclides are secured together by a derivatizing agent which is selected from the15. A composition of matter in accordance with claim 1 wherein said **antibody** is a monoclonal **antibody** targeted to a specific antigenic material defining a specific diseased cell...

...composition of matter in accordance with claim 22 wherein said biological element is a monoclonal **antibody** targeted to a specific antigenic material defining a specific **cancer** cell...

...17. A composition of matter in accordance with claim 1 wherein said **antibody**, said first nuclide and said second nuclide form a drug unit which is targeted to...

...19. The composition of matter in accordance with claim 1 including a plurality of **antibodies** secured to said drug unit...

...21. A composition of matter comprising: (a) a drug unit containing an **antibody** targeted to a specific antigen existing in a living being, and a first quantity of a first normally non-radioactive nuclide combined with said **antibody**, (b) said first nuclide capable of being rendered radioactive with radiation generated externally of said ...radiation when activated in one or more forms of atomic radiation of the group including **alpha particles**, beta **particles**, protons, gamma rays, positrons, antiprotons and the like...

...living being, said method comprising: (a) forming a plurality of drug units, each containing an **antibody** which is targeted to a specific antigen associated with such malady wherein each of said...

...to antigenic material at a site in the body of said living being when the **antibodies** of said drug units attach to respective antigens at said site, (c) monitoring said site...
...29. A method in accordance with claim 28 wherein said malady is defined by a **tumor** at said site and wherein the radioactivity generated by the nuclide material rendered radioactive by said beam of radiation directed at said site is operable to destroy said **tumor**.
...normally inactive nuclide is operable, when activated, to generate radioactivity selected from the forms of **radioactivity** including **alpha particles**, beta **particles**, protons, positrons, gamma rays, antiprotons and the like...

...36. A method in accordance with claim 35 wherein said site includes **cancer** cells which contain the antigen to which the **antibodies** of said drug units are targeted, and the steps of the method are **repeated** as many times as necessary to effect remission or destruction of the **tumor**.
...

...administering an additional quantity of said drug units to the body of said living being, **repeating** the monitoring step after allowing said additional units to target to antigenic material at said...

...39. A method in accordance with claim 38 wherein said site includes a **malignancy** defined by one or more cancerous tumors...
...accordance with claim 40 wherein said antigenic material is associated with the cells of a **tumor** at said site, and the image generated defines the shape and location of said **tumor**.
?

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? ds

Set     Items   Description
S1        202   BISMUTH(W)213 OR BI(W)213
S2     318925   ADVANTAG?
S3          6   S1 AND S2
S4          5   RD (unique items)
? s bismuth(w)212 or bi(w)212
          31935  BISMUTH
          18082  212
            101  BISMUTH(W)212
         563750  BI
          18082  212
            146  BI(W)212
      S5    237  BISMUTH(W)212 OR BI(W)212
? s s1 and s5
            202  S1
            237  S5
      S6     31  S1 AND S5
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
      S7     26  RD (unique items)
? s s7 and py<=1998
Processing
Processing
             26  S7
       33496537  PY<=1998
      S8     10  S7 AND PY<=1998
? t s8/3,k,ab/1-10

 8/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09912293   98391728   PMID: 9724387
  Radioimmunotherapy with alpha-emitting nuclides.
  McDevitt MR; Sgouros G; Finn RD; Humm JL; Jurcic JG; Larson SM;
Scheinberg DA
  Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.
  European journal of nuclear medicine (GERMANY)   Sep 1998,  25  (9)
  p1341-51,  ISSN 0340-6997   Journal Code: ENC
  Languages: ENGLISH
  Document type: Journal Article; Review; Review, Tutorial
  Record type: Completed
  This review discusses the application of alpha particle-emitting
radionuclides in targeted radioimmunotherapy. It will outline the
production and chemistry of astatine-211, bismuth-212 ,
lead-212, actinium-225, bismuth-213 , fermium-255, radium-223
and terbium-149, which at present are the most promising alpha-emitting
isotopes available for human clinical use. The selective cytotoxicity
offered by alpha particle-emitting radioimmunoconstructs is due to the high
linear energy transfer and short particle path length of these
radionuclides. Based upon the pharmacokinetics of alpha particle-emitting
radioimmunoconstructs, both stochastic and conventional dosimetric
methodology is discussed, as is the preclinical and initial clinical use of
these radionuclides conjugated to monoclonal antibodies for the treatment
of human neoplasia.

  Sep 1998,
  ...emitting radionuclides in targeted radioimmunotherapy. It will outline
the production and chemistry of astatine-211, bismuth-212,
lead-212, actinium-225, bismuth-213 , fermium-255, radium-223
```

and terbium-149, which at present are the most promising alpha...

8/3,K,AB/2 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

07229936 Genuine Article#: 139CM Number of References: 1
Title: Four-dimensional triple coincidence scintillation time spectrometer with two detectors (ABSTRACT AVAILABLE)
Author(s): Morozov VA (REPRINT) ; Churin IN; Kalinnikov VG; Morozova NV; Norseev YV
Corporate Source: JOINT INST NUCL RES,/DUBNA 141980/MOSCOW OBLAST/RUSSIA/ (REPRINT)
Journal: INSTRUMENTS AND EXPERIMENTAL TECHNIQUES, **1998**, V41, N5 (SEP-OCT), P614-618
ISSN: 0020-4412 Publication date: 19980900
Publisher: PLENUM PUBL CORP, CONSULTANTS BUREAU, 233 SPRING ST, NEW YORK, NY 10013
Language: English Document Type: ARTICLE
Abstract: A four-dimensional (4D) triple coincidence scintillation time spectrometer with two detectors, based on the previously reported autocorrelation single-crystal spectrometer, is intended for searching the isomeric states and the related cascade gamma-transitions in short-lived nuclei in the nano- and microsecond lifetime range. Half-lives were measured for the short-lived ground states of **Bi-212** and **Bi-213** nuclei and the isomeric states of decaying Yb-169 nuclei in the range of lifetimes T-1/2 = 0.3-3.7 mu s. The energy spectra of triple coincidences were studied.

, **1998**
...Abstract: and microsecond lifetime range. Half-lives were measured for the short-lived ground states of **Bi-212** and **Bi-213** nuclei and the isomeric states of decaying Yb-169 nuclei in the range of lifetimes...

8/3,K,AB/3 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06533503 Genuine Article#: YZ528 Number of References: 24
Title: Generator-produced alpha-emitters (ABSTRACT AVAILABLE)
Author(s): Mirzadeh S (REPRINT)
Corporate Source: OAK RIDGE NATL LAB,NUCL MED GRP, LIFE SCI RES DIV/OAK RIDGE//TN/37831 (REPRINT)
Journal: APPLIED RADIATION AND ISOTOPES, **1998**, V49, N4 (APR), P 345-349
ISSN: 0969-8043 Publication date: 19980400
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, ENGLAND OX5 1GB
Language: English Document Type: ARTICLE
Abstract: This review briefly describes the nuclear characteristics and production parameters for 7.2. h At-211, 60.6 min **Bi-212**, 45.6 min **Bi-213**, 11 d(233)Ra, and 20 h Fm-255. These alpha-emitting radioisotopes are the subject of current interest for alpha-particle-mediated radioimmunotherapy. Published by Elsevier Science Ltd.

, **1998**
...Abstract: the nuclear characteristics and production parameters for 7.2. h At-211, 60.6 min **Bi-212**, 45.6 min **Bi-213**, 11 d(233)Ra, and 20 h Fm-255. These alpha-emitting radioisotopes are the ...

...Identifiers--ANTIBODY; **BI-212**; RADIOIMMUNOTHERAPY; THERAPY; PB-212

8/3,K,AB/4 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06332173 Genuine Article#: YJ421 Number of References: 28
Title: Bi-labelled antibody and bi-labelled streptavidin. Comparison of targeting efficacy of a lymphoma cell line in vitro (ABSTRACT AVAILABLE)
Author(s): Henriksen G (REPRINT) ; Funderud S; Hoff P
Corporate Source: UNIV OSLO,DEPT CHEM, POB 1033 BLINDERN/N-0315 OSLO//NORWAY/ (REPRINT); NORWEGIAN RADIUM HOSP,IMMUNOL SECT/N-0310 OSLO//NORWAY/
Journal: JOURNAL OF LABELLED COMPOUNDS & RADIOPHARMACEUTICALS, **1997**, V39, N12 (DEC), P1039-1046
ISSN: 0362-4803 Publication date: 19971200
Publisher: JOHN WILEY & SONS LTD, BAFFINS LANE CHICHESTER, W SUSSEX, ENGLAND PO19 1UD
Language: English Document Type: ARTICLE
Abstract: An anti-lymphoma antibody (HH-1) and streptavidin were conjugated with the chelator CHX-A DTPA add subsequently labelled with Bi-205,Bi-206. The immunoreactivity of the antibody to the target antigen and the binding ability of streptavidin to antigen-bound biotinylaled HH-1 were then investigated at different degrees of chelator content. Streptavidin was shown to be more tolerant than HH-1 towards the chelator modification. While the binding reactivity of HH-1 decreased to 60% at an average of 3.5 chelators per molecule, the 60% level was obtained at an average of 6.5 chelators per streptavidin molecule. Streptavidin may therefore possibly be used to obtain **Bi-212**,**Bi-213**-labelled compounds for alpha-particle radiotherapy with higher specific activity.

, **1997**
...Abstract: of 6.5 chelators per streptavidin molecule. Streptavidin may therefore possibly be used to obtain **Bi-212**,**Bi-213**-labelled compounds for alpha-particle radiotherapy with higher specific activity.

8/3,K,AB/5 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04496779 Genuine Article#: TH916 Number of References: 20
Title: RADIOLABELED ANTI-CD33 MONOCLONAL-ANTIBODY M195 FOR MYELOID LEUKEMIAS (Abstract Available)
Author(s): JURCIC JG; CARON PC; NIKULA TK; PAPADOPOULOS EB; FINN RD; GANSOW OA; MILLER WH; GEERLINGS MW; WARRELL RP; LARSON SM; SCHEINBERG DA
Corporate Source: MEM SLOAN KETTERING CANC CTR,LEUKEMIA SERV,1275YORK AVE/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR,DEV CHEMOTHERAPY SERV/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR,BONE MARROW TRANSPLANT SERV/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR,DEPT MED/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR,DEPT RADIOL,NUCL MED SERV/NEW YORK//NY/10021; NCI,RADIAT ONCOL BRANCH,CHEM SECT/BETHESDA//MD/20892; PHARMACTINIUM INC/WILMINGTON//DE/00000
Journal: CANCER RESEARCH, **1995**, V55, N23 (DEC 1), PS5908-S5910
ISSN: 0008-5472
Language: ENGLISH Document Type: ARTICLE
Abstract: M195, a mouse monoclonal antibody reactive with the early myeloid antigen CD33, has been shown to target leukemia cells in patients and to reduce large leukemic burdens when labeled with I-131, A

complementarity-determining region-grafted, humanized version (HuM195) has demonstrated similar targeting of leukemia cells without immunogenicity, We have studied two applications of therapy with I-131-M195. First, to intensify therapy prior to bone marrow transplantation (BMT), we combined I-131-M195 with busulfan and cyclophosphamide, Fifteen patients received first BMT for relapsed or refractory acute myelogenous leukemia or accelerated or blastic chronic myelogenous leukemia; four received second BMT for relapsed chronic or accelerated chronic myelogenous leukemia. Doses of I-131-M195 ranged from 120 to 230 mCi/m(2). Few toxicities could be attributed to I-131-M195 therapy, and all patients engrafted, Eighteen patients achieved complete remission, Among those patients receiving first BMT, three have remained in unmaintained remission for 18+ to 29+ months, Six patients relapsed, including one with isolated central nervous system disease 32 months after BMT, Ten patients died in complete remission of transplant-related complications, Second, we studied whether I-131-M195 could reduce minimal residual disease and prolong remission and survival durations safely in patients with relapsed acute promyelocytic leukemia after they attained remission with all-trans-retinoic acid. Seven patients were treated with either 50 or 70 mCi/m(2) I-131-M195, Toxicity was limited to myelosuppression, As a measure of minimal residual disease, we monitored PML/RAR-alpha mRNA by reverse transcription PCR, Six patients had positive reverse transcription PCR assays prior to receiving I-131-M195; two converted transiently to negative, Median disease-free survival and overall survival of the seven patients were 8 (range, 3-14.5) months and 28 (range, 5.5-43+) months, respectively. This regimen compares favorably with others for relapsed acute promyelocytic leukemia, In an effort to avoid nonspecific cytotoxicity associated with I-131 in future trials for minimal residual disease, we have conjugated short-range, alpha particle-emitting radioisotopes to HuM195 using a bifunctional chelate, 2-(p-isothiocyanatobenzyl)-cyclohexyldiethyl- enetriaminepentaacetic acid, with high efficiency and specific activities, **Bi-212** -HuM195 has demonstrated dose- and specific activity-dependent killing of HL60 cells in vitro, Injection of **Bi-213**-HuM195 into healthy BALB/c mice produced no effects on weight or viability.

, **1995**
...Abstract: a bifunctional chelate, 2-(p-isothiocyanatobenzyl)-cyclohexyldiethyl- enetriaminepentaacetic acid, with high efficiency and specific activities, **Bi-212** -HuM195 has demonstrated dose- and specific activity-dependent killing of HL60 cells in vitro, Injection of **Bi-213**-HuM195 into healthy BALB/c mice produced no effects on weight or viability.

8/3,K,AB/6 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04079741 Genuine Article#: RC713 Number of References: 0
(NO REFS KEYED)
Title: CYTOTOXICITY OF **BI-213**-IMMUNOCONJUGATES AND AC-225-IMMUNOCONJUGATES (Abstract Available)
Author(s): KASPERSEN FM; BOS E; DOORNMALEN AV; GEERLINGS MW; APOSTOLIDIS C; MOLINET R
Corporate Source: NV ORGANON,POB 20/5340 BH OSS//NETHERLANDS/; NV ORGANON/5340 BH OSS//NETHERLANDS/
Journal: NUCLEAR MEDICINE COMMUNICATIONS, **1995**, V16, N6 (JUN), P 468-476
ISSN: 0143-3636
Language: ENGLISH Document Type: ARTICLE
Abstract: This paper describes in vitro cytotoxicity experiments with **Bi-213**- and Ac-225-immunoconjugates on the human epidermoid

tumour cell line A431 using a blood group A-reactive murine IgG (2D11) as the specific antibody and MOPC 21 as the control antibody. With both radionuclides, specific cell-killing was achieved. The observed cytotoxicity of **Bi-213** (T-1/2 = 47 min) indicates that this radionuclide is a useful alternative for the alpha-emitter **Bi-212** in the treatment of blood-borne malignancies. Ac-225-immunoconjugates (T-1/2 of (225)AC is 10 days) may be applicable for the treatment of solid rumours, since the daughter radionuclides of (225)AC contribute to the cytotoxic efficacy by a field effect (i.e. toxicity in an area distal from the antibody-binding site). The lack of an adequate chelator for (225)AC is a major drawback.

Title: CYTOTOXICITY OF **BI-213**-IMMUNOCONJUGATES AND AC-225-IMMUNOCONJUGATES
, **1995**
Abstract: This paper describes in vitro cytotoxicity experiments with **Bi-213**- and Ac-225-immunoconjugates on the human epidermoid tumour cell line A431 using a blood...

...the control antibody. With both radionuclides, specific cell-killing was achieved. The observed cytotoxicity of **Bi-213** (T-1/2 = 47 min) indicates that this radionuclide is a useful alternative for the alpha-emitter **Bi-212** in the treatment of blood-borne malignancies. Ac-225-immunoconjugates (T-1/2 of (225...

8/3,K,AB/7 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

02108364 Genuine Article#: KB552 Number of References: 9
Title: GROUND-STATE MAGNETIC-MOMENTS OF **BI-212**,**BI-213** (Abstract Available)
Author(s): LINDROOS M; RICHARDS P; BLOMQVIST J; RIKOVSKA J; STONE NJ
Corporate Source: CHALMERS UNIV TECHNOL,DEPT PHYS/S-41296 GOTHENBURG//SWEDEN/; UNIV OXFORD,CLARENDON LAB,DEPT PHYS/OXFORD//ENGLAND/; MANNE SIEGBAHN INST PHYS/S-10405 STOCKHOLM//SWEDEN/
Journal: HYPERFINE INTERACTIONS, **1992**, V75, N1-4, P109-116
ISSN: 0304-3843
Language: ENGLISH Document Type: ARTICLE
Abstract: The magnetic dipole moments of **Bi-212** and **Bi-213** have been measured and the results are interpreted within the framework of the shell model.

Title: GROUND-STATE MAGNETIC-MOMENTS OF **BI-212**,**BI-213**
, **1992**
Abstract: The magnetic dipole moments of **Bi-212** and **Bi-213** have been measured and the results are interpreted within the framework of the shell model.

8/3,K,AB/8 (Item 1 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

05541050 Genuine Article#: RV105 Number of References: 0
Title: PRODUCTION OF BI-211,**BI-212**,**BI-213** FROM PB, T1, AND HG BY O-18 IONS
Author(s): ESKOLA K; ESKOLA P; FOWLER MM; OHM H; TREHER EN; WILHELMY JB
Corporate Source: UNIV CALIF LOS ALAMOS NATL LAB/LOS ALAMOS//NM/87545
Journal: ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, **1983**, V186, AUG, P44-NUCL

Language: ENGLISH Document Type: MEETING ABSTRACT

Title: PRODUCTION OF BI-211,**BI-212**,**BI-213** FROM PB,
T1, AND HG BY O-18 IONS
, **1983**

8/3,K,AB/9 (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 2680208 IFI Acc No: 9600860
Document Type: C
DETECTION AND THERAPY OF LESIONS WITH BIOTIN/AVIDIN POLYMER CONJUGATES
Inventors: Griffiths Gary L (US)
Assignee: Immunomedics Inc
Assignee Code: 14427
Publication (No,Date), Applic (No,Date):
US 5482698 **19960109** US 9351144 19930422
Publication Kind: A
Calculated Expiration: 20130422
(Cited in 010 later patents)
Priority Applic(No,Date): US 9351144 19930422

Abstract: Methods of detecting and/or treating lesions in a patient are provided. The methods are an improvement over known methods comprising the steps of (a) parenterally injecting a subject with a targeting composition comprised of a biotin-protein conjugate or an avidin-protein conjugate, wherein the protein preferentially binds to a marker substance produced or associated with the targeted lesion, and allowing the protein conjugate to preferentially accrete at the targeted lesion; (b) then parenterally injecting a clearing composition comprised of (i) avidin, when the targeting composition is a biotin-protein conjugate, or (ii) biotin, when the targeting composition is a avidin-protein conjugate, and allowing the clearing composition to substantially clear the targeting composition from nontargeted sites and to bind to the targeting composition accreted at the targeted lesion; and (c) parenterally injecting a detection or therapeutic composition comprised of a conjugate of (i) avidin and detection or therapeutic agent when the clearing composition is biotin, or (ii) biotin and detection or therapeutic agent when the clearing agent is avidin, and allowing the composition to accrete at the targeted lesion. The improvement is having at least one of the compositions of step (a) or (b) further comprise a polymer to which multiple moieties of avidin or biotin can conjugate, thereby providing an increased number of binding sites to which a subsequently administrated composition can bind thereby amplifying the amount of detection or therapeutic agent at the targeted site.

Publication (No,Date), Applic (No,Date):
...**19960109**
Non-exemplary Claims: ...therapeutic agent is an isotope which is one of
Iodine-125, Iodine-131, Actinium-225, **Bismuth-212**,
Bismuth-213, Lead-212, Rhenium-186, Rhenium-188, Silver-111,
Platinum-197, Palladium-109, Copper-67, Phosphorus...

8/3,K,AB/10 (Item 2 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 1528011 IFI Acc No: 8410307
Document Type: C
USE OF METAL CHELATE CONJUGATED MONOCLONAL ANTIBODIES; DIAGNOSIS, TREATMENT
OF CANCER

Inventors: GANSOW OTTO A (US); STRAND METTE (US)
Assignee: UNASSIGNED OR ASSIGNED TO INDIVIDUAL
Assignee Code: 68000 Document Type: REASSIGNED
Publication (No,Date), Applic (No,Date):
US 4454106 **19840612** US 82386109 19820607
Publication Kind: A
Calculated Expiration: 20020607
(Cited in 071 later patents) Document Type: CERTIFICATE OF CORRECTION
Certificate of Correction Date: 19841120
Priority Applic(No,Date): US 82386109 19820607

Abstract: Therapeutic and diagnostic methods employing metal chelate conjugated monoclonal antibodies are described. Metals employed in therapeutic conjugated antibodies include alpha particle, beta particle or Auger electron emitting isotopes. Diagnostic methods may be either in vivo or in vitro. Chelated metals employed in diagnostic techniques may include, inter alia, gamma or positron emitting metals as well as fluorogenic or paramagnetic metals.

Publication (No,Date), Applic (No,Date):
...**19840612**
Non-exemplary Claims: ...of claim 2 wherein said radiometal is selected from the group consisting of Bi-211, **Bi-212** and **Bi-213**.
...

...4. The method of claim 3 wherein said radiometal is **Bi-212**.
...

...9. The method of claim 6 wherein said radiometal is **Bi-212** and the metal chelate conjugated monoclonal antibody solution has at least about 98% of the
?

Radionuclides for radioimmunotherapy: Criteria for selection.
AUTHOR: Geerling M W
AUTHOR ADDRESS: Akzo nv, P.O. Box 9300, 6800 Arnhem**Netherlands
JOURNAL: International Journal of Biological Markers 8 (3):p180-186
1993
ISSN: 0393-6155
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In developing and designing radioimmunotherapy, the selection of the isotope is a major factor. This selection depends on a number of criteria and parameters, affecting usefulness and feasibility. Usefulness is directly related to the radiological performance of the ionising radiation in relation to tissue and its morphology, with a major distinction between the effects of alpha and beta-particles (or rays). Usefulness is also directly related to the pharmacodynamic performance of the isotope-carrier (e.g. **antibody**) complex, where the proper choice of isotope radiodecay halflife is of major importance. Feasibility depends on availability of the components in the isotope-ligand-carrier complex, and also on convenience and safety aspects in the preparation and the handling of the materials as well as in their application inpatients. A comparison is made between the various properties of alpha-emitting isotopes that have been proposed over a number of years, concluding that the combination 225Ac- 213Bi deserves serious further attention.

1993

1993

...ABSTRACT: Usefulness is also directly related to the pharmacodynamic performance of the isotope-carrier (e.g. **antibody**) complex, where the proper choice of isotope radiodecay halflife is of major importance. Feasibility depends...
...REGISTRY NUMBERS: **BISMUTH-213**
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: ...**BISMUTH-213**
MISCELLANEOUS TERMS: ...**BISMUTH-213**; ...

...**CANCER** TREATMENT

7/3,K,AB/4 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06492753 Genuine Article#: YW901 Number of References: 30
Title: Vascular targeting for radioimmunotherapy with **Bi-213** (ABSTRACT AVAILABLE)
Author(s): Kennel SJ (REPRINT) ; Mirzadeh S
Corporate Source: OAK RIDGE NATL LAB,DIV LIFE SCI/OAK RIDGE//TN/37831 (REPRINT)
Journal: RADIOCHIMICA ACTA, **1997**, V79, N2, P87-91
ISSN: 0033-8230 Publication date: 19970000
Publisher: R OLDENBOURG VERLAG, LEKTORAT M/N, K BERBER-NERLINGER, POSTFACH 80 13 60, D-81613 MUNCHEN, GERMANY
Language: English Document Type: ARTICLE
Abstract: Effective targeting of short-lived a-emitters such as **Bi-213** can be accomplished only with agents that localize rapidly. One such approach uses MAbs that bind to the luminal side of **tumor** vasculature. MAbs 34A and 201B bind to murine thrombomodulin which is found in lung endothelium. These MAbs were derivatized with CHXb-DTPA and bound **Bi-213**. The labeled

MAbs were shown to deliver over 50% of the injected dose to mouse lungs. The **Bi-213** remained in the lungs with a t(1/2) > 4 h, and there was only slight deposition of isotope at other sites (kidney, liver, spleen). **Bi-213** coupled to MAb was shown to kill **tumor** cells in tissue culture efficiently. Injection of large doses (600 mu Ci) of **Bi-213** MAb 201 into mice that had previously been injected with EMT-6 **tumor** cells to form lung colonies resulted in hemorrhage in **tumor** and normal lung tissue at 4 days post injection. Lower doses (<300 mu Ci/animal) were better tolerated in normal tissue. Successful targeting of **Bi-213** to **tumor** vasculature has been accomplished in this model system and has significant promise for therapy in humans when appropriate targeting reagents are identified.

Title: Vascular targeting for radioimmunotherapy with **Bi-213**, **1997**

Abstract: Effective targeting of short-lived a-emitters such as **Bi-213** can be accomplished only with agents that localize rapidly. One such approach uses MAbs that bind to the luminal side of **tumor** vasculature. MAbs 34A and 201B bind to murine thrombomodulin which is found in lung endothelium. These MAbs were derivatized with CHXb-DTPA and bound **Bi-213**. The labeled MAbs were shown to deliver over 50% of the injected dose to mouse lungs. The **Bi-213** remained in the lungs with a t(1/2) > 4 h, and there was only slight deposition of isotope at other sites (kidney, liver, spleen). **Bi-213** coupled to MAb was shown to kill **tumor** cells in tissue culture efficiently. Injection of large doses (600 mu Ci) of **Bi-213** MAb 201 into mice that had previously been injected with EMT-6 **tumor** cells to form lung colonies resulted in hemorrhage in **tumor** and normal lung tissue at 4 days post injection. Lower doses (<300 mu Ci/animal) were better tolerated in normal tissue. Successful targeting of **Bi-213** to **tumor** vasculature has been accomplished in this model system and has significant promise for therapy in...

...Identifiers--MONOCLONAL-**ANTIBODY**; **TUMOR**-GROWTH; ALPHA-PARTICLES; SOLID **TUMORS**; ANGIOGENESIS; INHIBITION; MICE; CELLS; INTERLEUKIN-2; METASTASIS

7/3,K,AB/5 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06332173 Genuine Article#: YJ421 Number of References: 28

Title: Bi-labelled **antibody** and bi-labelled streptavidin. Comparison of targeting efficacy of a lymphoma cell line in vitro (ABSTRACT AVAILABLE)

Author(s): Henriksen G (REPRINT) ; Funderud S; Hoff P
Corporate Source: UNIV OSLO,DEPT CHEM, POB 1033 BLINDERN/N-0315 OSLO//NORWAY/ (REPRINT); NORWEGIAN RADIUM HOSP,IMMUNOL SECT/N-0310 OSLO//NORWAY/

Journal: JOURNAL OF LABELLED COMPOUNDS & RADIOPHARMACEUTICALS, **1997**, V39, N12 (DEC), P1039-1046
ISSN: 0362-4803 Publication date: 19971200
Publisher: JOHN WILEY & SONS LTD, BAFFINS LANE CHICHESTER, W SUSSEX, ENGLAND PO19 1UD
Language: English Document Type: ARTICLE

Abstract: An anti-lymphoma **antibody** (HH-1) and streptavidin were conjugated with the chelator CHX-A DTPA add subsequently labelled with Bi-205,Bi-206. The immunoreactivity of the **antibody** to the target antigen and the binding ability of streptavidin to antigen-bound biotinylaled HH-1 were then investigated at different degrees of chelator content. Streptavidin was shown to be more tolerant than HH-1 towards the chelator modification. While the binding reactivity of HH-1

(NO REFS KEYED)

Title: A METHOD FOR STUDYING THE EFFECT OF THE DISTRIBUTION OF INHALED (PUO2)-PU-239 PARTICLES ON DOSE-RATE DISTRIBUTION IN THE BEAGLE DOG LUNG (Abstract Available)

Author(s): SHYR LJ; DIEL JH; CHANG IY; GUILMETTE RA
Corporate Source: INHALAT TOXICOL RES INST,POB 5890/ALBUQUERQUE//NM/87185

Journal: RADIATION PROTECTION DOSIMETRY, **1991**, V38, N1-3, P229-235
Language: ENGLISH Document Type: ARTICLE

Abstract: Dosimetric quantities that describe local dose distribution in the lung are needed to construct a more biologically relevant response model or to compensate for the limitations of the averaged dose to lung in predicting risks. To determine local dose distribution, the distribution of the irradiating sources (**alpha-emitting particles**), with respect to the structure of the lung, needs to be taken into account. We developed a method to calculate dose rate distributions based on observations of lung sections from dogs exposed to Pu. Random samples of 5-mu-m thick lung sections were taken from dogs sacrificed at different times after inhalation exposure to monodisperse aerosols of (PuO2)-Pu-239. The distributions of **alpha-track** length, energy deposition, and **particle** concentration were estimated based on the lung section data, and used to calculate the dose rate distribution in the lung. The derived dose rate distribution was compared with distributions generated by assuming that particles were randomly or uniformly distributed in the lung. The difference in the fraction of lung tissues in each dose rate category for different source distributions may prove to be an important factor in explaining the difference observed in lung responses for the same absorbed lung dose. Also discussed are the uncertainty associated with the derived dose rate distribution, and our future efforts to derive an analytical expression for the dose rate distribution.

02463422 Genuine Article#: LC965 Number of References: 9
Title: EVALUATION OF AN ALPHA-PROBE DETECTOR FOR INVITRO CELLULAR DOSIMETRY (Abstract Available)
Author(s): HUI TE; JAMES AC; JOSTES RF; SCHWARTZ JL; SWINTH KL; CROSS FT
Corporate Source: BATTELLE MEM INST,PACIFIC NW LABS,DEPT HLTH PHYS/RICHLAND//WA/99352; ARGONNE NATL LAB,DIV BIOL & MED RES/ARGONNE//IL/60439; BATTELLE MEM INST,PACIFIC NW LABS,DEPT BIOL & CHEM/RICHLAND//WA/99352
Journal: HEALTH PHYSICS, **1993**, V64, N6 (JUN), P647-652
ISSN: 0017-9078
Language: ENGLISH Document Type: ARTICLE
Abstract: This paper describes the design and testing of an alpha probe detector for the continuous measurement of the activity concentrations of alpha **emitters** in the culture media of in vitro cell suspension irradiation systems. The probe detector consists of a pen-size body housing a small silicon surface-barrier detector with a Mylar window. Theoretical calculations were performed to study the dependence of the alpha-energy spectrum on 1) the thickness of the Mylar barrier; 2) the Mylar-detector distance; and 3) the size of the detector window. These design parameters were selected by taking a compromise between the counting efficiency, the integrity of the detector, and its required range of application. The probe detector was tested using both chelated and unchelated Bi-212 and Pb-212 standard solutions; plate-out of these radionuclides on the Mylar barrier was observed for unchelated solutions. Alpha energy spectra were analyzed using a total integration technique. The measured activity concentrations and the calibrated values agree to within 4% for the chelated B-212 and to within 6% for the unchelated Bi-212. The alpha probe detector can be used throughout an entire exposure time period to determine the total dose received by suspended cells, or at different time intervals to determine the dose rate in real time.

, **1993**